

 A large, abstract graphic on the left side of the slide consists of several thick, curved lines in various colors (teal, green, orange, grey, light blue) arranged in a circular pattern, resembling a stylized sunburst or a cluster of paths.

EPICS















Global Perspectives in Gastrointestinal Malignancies in 2024

July 8 and 12, 2024

Full report

Report Contents

EPICS

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
July 8 and 12, 2024



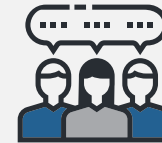
**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
GI cancer
> 5 from US
> 3 from Europe



**GI CANCER-SPECIFIC
DISCUSSIONS** on latest
research updates, therapeutic
advances, and their
application in clinical
decision-making

Panel Consisting of 8 Global GI Cancer Experts

EPICS

Nataliya Uboha, MD, PhD
University of Wisconsin Madison



Kristen Ciombor, MD
Vanderbilt University Medical Center



Efrat Dotan, MD
Fox Chase Cancer Center



CHAIR:
Howard S. Hochster, MD
Rutgers Cancer Institute of
New Jersey



Julien Taieb, MD, PhD
Université de Paris



Gerald Prager, MD
Medical University of Vienna



Dirk Arnold, MD, PhD
University of Hamburg



Tanios Bekaii-Saab, MD, FACP
Mayo Clinic Cancer Center



Meeting Agenda: Day 1

EPICS

Time (ET/CEST)	Topic	Speaker/Moderator
9.30 AM – 9.35 AM/15.30 – 15.35	Welcome and Introductions	Howard Hochster, MD
9.35 AM – 9.45 AM/15.35 – 15.45	Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments	Dirk Arnold, MD, PhD
9.45 AM – 10.15 AM/15.45 – 16.15	Discussion	All
10.15 AM – 10.20 AM/16.15 – 16.20	Key Takeaways	Dirk Arnold, MD, PhD
10.20 AM – 10.30 AM/16.20 – 16.30	Colorectal Cancer – Immunotherapy	Julien Taieb, MD, PhD
10.30 AM – 11.00 AM/16.30 – 17.00	Discussion	All
11.00 AM – 11.05 AM/17.00 – 17.05	Key Takeaways	Julien Taieb, MD, PhD
11.05 AM – 11.25 AM/17.05 – 17.25	ctDNA Updates and Integration in Clinical Practice	Howard Hochster, MD
11.25 AM – 11.35 AM/17.25 – 17.35	BREAK	All
11.35 AM – 11.50 AM/17.35 – 17.50	Rectal Cancer	Kristen Ciombor, MD
11.50 AM – 12.20 PM/17.50 – 18.20	Discussion	All
12.20 PM – 12.25 PM/18.20 – 18.25	Key Takeaways	Kristen Ciombor, MD
12.25 PM – 12.30 PM/18.25 – 18.30	Summary and Closing Remarks	Howard Hochster, MD



Meeting Agenda: Day 2

EPICS

Time (ET/CEST)	Topic	Speaker/Moderator
9.30 AM – 9.35 AM/15.30 – 15.35	Welcome and Introductions	Howard Hochster, MD
9.35 AM – 9.45 AM/15.35 – 15.45	Gastroesophageal Junction (GEJ) and Gastric Cancer	Nataliya Uboha, MD, PhD
9.45 AM – 10.10 AM/15.45 – 16.10	Discussion	All
10.10 AM – 10.15 AM/16.10 – 16.15	Key Takeaways	Nataliya Uboha, MD, PhD
10.15 AM – 10.25 AM/16.15 – 16.25	Hepatocellular Carcinoma (HCC)	Tanios Bekaii-Saab, MD, FACP
10.25 AM – 10.45 AM/16.25 – 16.45	Discussion	All
10.45 AM – 10.50 AM/16.45 – 16.50	Key Takeaways	Tanios Bekaii-Saab, MD, FACP
10.50 AM – 11.00 AM/16.50 – 17.00	BREAK	All
11.00 AM – 11.10 AM/17.00 – 17.10	Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)	Howard Hochster, MD
11.10 AM – 11.20 AM/17.10 – 17.20	Pancreatic Cancer	Efrat Dotan, MD
11.20 AM – 11.40 AM/17.20 – 17.40	Discussion	All
11.40 AM – 11.45 AM/17.40 – 17.45	Key Takeaways	Efrat Dotan, MD
11.45 AM – 11.55 AM/17.45 – 17.55	Biliary Tract Cancer	Gerald Prager, MD
11.55 AM – 12.20 PM/17.55 – 18.20	Discussion	All
12.20 PM – 12.25 PM/18.20 – 18.25	Key Takeaways	Gerald Prager, MD
12.25 PM – 12.30 PM/18.25 – 18.30	Summary and Closing Remarks	Howard Hochster, MD



EPICS

Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker- Driven Treatments



Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (1/3)

Presented by Dirk Arnold, MD, PhD

Highlights From Recent Congresses

Hyperselection and anti-EGFR therapy

STUDY POPULATION

1000 patients with metastatic colorectal cancer... (text is blurred)

RESULTS

Median overall survival... (text is blurred)

KEY POINT CONCLUSIONS

Continuing... (text is blurred)

RESPONSE RATES BY BIOMARKER STATUS



RESPONSE RATES BY BIOMARKER STATUS AND TREATMENT





Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (2/3)

Presented by Dirk Arnold, MD, PhD

Highlights From Recent Congresses

Anti-EGFR + KRAS G12C inhibitors

CodeBreakK 300

STUDY POPULATION

1000 patients with KRAS G12C mutation... (text is blurred)

RESULTS

Median OS was 12.1 months... (text is blurred)

KEY CONCLUSIONS

Combining KRAS G12C inhibitor... (text is blurred)

RESPONSE RATES



RESPONSE RATES BY BIOMARKER STATUS





Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (3/3)

Presented by Dirk Arnold, MD, PhD

Highlights From Recent Congresses

New targets

STUDY POPULATION

1000 patients with metastatic colorectal cancer... (text is blurred)

RESULTS

Median overall survival... (text is blurred)

KEY POINT CONCLUSIONS

Continuing... (text is blurred)

RESPONSE RATES BY BIOMARKER STATUS



RESPONSE RATES BY BIOMARKER STATUS AND TIME PERIOD



EPICS

Key Insights

Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments

Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (1/3)

Overview of chemotherapy regimens for metastatic colorectal cancer

Chemotherapy is the mainstay of treatment for metastatic colorectal cancer. The most commonly used regimens include:

- FOLFOX:** A combination of fluorouracil (5-FU), leucovorin, and oxaliplatin.
- FOLFIRI:** A combination of fluorouracil (5-FU), leucovorin, and irinotecan.
- CAPOX:** A combination of capecitabine and oxaliplatin.

These regimens are typically given in cycles, with treatment breaks in between. The choice of regimen depends on the patient's overall health, previous treatments, and the extent of the disease.

Overview of targeted therapies for metastatic colorectal cancer

Targeted therapies are designed to block specific molecules that are involved in the growth and spread of cancer cells. These therapies are often used in combination with chemotherapy. The most commonly used targeted therapies for metastatic colorectal cancer include:

- Anti-EGFR antibodies:** Such as cetuximab and panitumumab, which block the epidermal growth factor receptor (EGFR).
- Anti-VEGF antibodies:** Such as bevacizumab, which blocks vascular endothelial growth factor (VEGF).
- Anti-HMGB2 antibody:** Such as regorafenib, which blocks the hepatocyte growth factor receptor (HGFR).

Targeted therapies can improve outcomes in certain patients, but they are not effective for everyone. Biomarker testing is used to identify patients who are most likely to benefit from these therapies.

Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (2/3)

Targeted therapies will help identify the optimal sequencing of agents

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Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (3/3)

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EPICS

Colorectal Cancer – Immunotherapy



Colorectal Cancer – Immunotherapy (1/3)

Presented by Julien Taieb, MD, PhD

Highlights From Recent Congresses

MSI-H mCRC

CheckMate 8HW – PFS2

STUDY POPULATION

MSI-H mCRC study: 4577 patients with a 50% high heterozygosity of dMMR and a 50% mismatch with 1688 genes in tumor tissues, not matching MSS, heterozygosity to dMMR, or tumor average 50% heterozygosity. Median OS was 10.5 months in the treatment with pembrolizumab compared with 7.3 months in the treatment with chemotherapy (HR 0.82, 95% CI 0.69-0.98, P=0.027). The study is ongoing. 4577 patients with 1688 genes in dMMR. Median OS was 10.5 months in the treatment with pembrolizumab compared with 7.3 months in the treatment with chemotherapy. The study is ongoing.

RESULTS

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KEY CONCLUSIONS

Treatment with pembrolizumab showed better OS compared with chemotherapy in MSI-H mCRC patients and decreased the maintenance need in patients.

OS PROBABILITIES FROM DAY 0 TO 560 DAYS IN THE TREATMENT WITH PFS2



RESPONSE RATES AT VARIOUS ANALYSIS POINTS





Colorectal Cancer – Immunotherapy (2/3)

Presented by Julien Taieb, MD, PhD

Highlights From Recent Congresses

MSI-H early-stage CRC (cont.)

FFCD 1703 POCHI

STUDY POPULATION

1. 100 patients with MSI-H early-stage CRC (cont.)

2. 100 patients with MSI-H early-stage CRC (cont.)

3. 100 patients with MSI-H early-stage CRC (cont.)

4. 100 patients with MSI-H early-stage CRC (cont.)

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9. 100 patients with MSI-H early-stage CRC (cont.)

10. 100 patients with MSI-H early-stage CRC (cont.)

RESULTS

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10. 100 patients with MSI-H early-stage CRC (cont.)

KEY POINT CONCLUSIONS

1. 100 patients with MSI-H early-stage CRC (cont.)

2. 100 patients with MSI-H early-stage CRC (cont.)

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10. 100 patients with MSI-H early-stage CRC (cont.)

RESPONSE RATES AND TOXICITY



RESPONSE RATES AND TOXICITY





Colorectal Cancer – Immunotherapy (3/3)

Presented by Julien Taieb, MD, PhD

Highlights From Recent Congresses

New targets

ARC9

STUDY POPULATION

1. 1000 patients with metastatic colorectal cancer (mCRC) were randomized to receive either the investigational drug (n=500) or standard of care (n=500). The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoint was OS at 48 weeks. The tertiary endpoint was OS at 72 weeks. The study was designed to evaluate the efficacy and safety of the investigational drug in patients with mCRC. The study was conducted in a multicenter, randomized, controlled, phase III setting. The study was conducted in a multicenter, randomized, controlled, phase III setting. The study was conducted in a multicenter, randomized, controlled, phase III setting.

RESULTS

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KEY CONCLUSIONS

1. The investigational drug demonstrated a statistically significant improvement in OS compared to standard of care. The study was designed to evaluate the efficacy and safety of the investigational drug in patients with mCRC. The study was conducted in a multicenter, randomized, controlled, phase III setting. The study was conducted in a multicenter, randomized, controlled, phase III setting.

ARC9: PHASE III STUDY OF THE EFFICACY AND SAFETY OF THE INVESTIGATIONAL DRUG IN PATIENTS WITH METASTATIC COLORECTAL CANCER



RESPONSE RATES AND SAFETY PROFILE



EPICS

Key Insights

Colorectal Cancer – Immunotherapy

Colorectal Cancer – Immunotherapy (1/3)

Immunotherapy will help identify the optimal sequencing of agents

- 1. Treatment will start with a combination of immunotherapy agents, such as pembrolizumab and nivolumab, followed by TIGIT inhibitors, for most patients
- 2. These agents are being investigated in combination therapies, but will probably be used sequentially for patients with evidence of tumor resistance
- 3. The sequential approach may also be used in the neoadjuvant setting, before TIGIT, for patients with documented tumor resistance
 - Planned to test sequential agents are divided on whether they would normally use TIGIT or immunological checkpoint inhibitors
 - Results of the ongoing IM-151 trial (described in accompanying immunological checkpoint in TIGIT) will help to clarify the optimal sequencing of these agents
- 4. Immunological checkpoint and the sequential approach may also be used earlier than starting a patient who never following treatment with immunological checkpoint and TIGIT in the neoadjuvant setting, but this represents a small fraction of patients
- 5. Future approaches can also focus on the sequencing of these two agents (eg. 1 drug or 1 drug, versus about how long to combine)
- 6. The sequential efficacy of immunological checkpoint and the sequential approach have opened other options, such as immunological checkpoint combinations, nivolumab and ipilimumab, in the form of therapy



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Colorectal Cancer – Immunotherapy (2/3)

Immunotherapy will help modify the immune responsiveness of agents

- 1. Treatment can start with a combination of the immune system modulators and conventional therapy, followed by TDMT afterwards, for most patients
- 2. Most agents are using immunomodulatory antibodies, but will probably be modified later for patients with evidence of tumor resistance
- 3. The modified agent may also be used in the second-line setting, before TDMT, for patients with documented tumor resistance
 - 1. Provided a good supportive regimen are decided on whether they would normally use TDMT or immunomodulatory antibodies
 - 2. Results of the ongoing IM-131 trial suggests that combining immunomodulatory antibodies as TDMT will help to modify the immune responsiveness of these agents
- 4. Immunomodulatory antibodies and the modified agent may also be used earlier than starting a patient who never following treatment with immunomodulatory antibodies and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient performance can also factor into the sequencing of these two agents eg. 2 drugs in 1 drug regimen about how well is tolerated
- 6. The immunologic efficacy of immunomodulatory antibodies and the modified agents have opened other options, such as immunomodulatory chemotherapy combinations, vaccines, and adoptive cell transfer of therapy



Immunotherapy will help modify the immune responsiveness of agents

Most agents are using immunomodulatory antibodies, but will probably be modified later for patients with evidence of tumor resistance

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Patient performance can also factor into the sequencing of these two agents eg. 2 drugs in 1 drug regimen about how well is tolerated

The immunologic efficacy of immunomodulatory antibodies and the modified agents have opened other options, such as immunomodulatory chemotherapy combinations, vaccines, and adoptive cell transfer of therapy



Immunotherapy in early-stage disease

Checkpoints in immunotherapy: immune response to cancer

Immunotherapy works by helping the immune system recognize and attack cancer cells. The immune system has cells that can identify and kill cancer cells, but sometimes cancer cells can hide from the immune system. Immunotherapy helps by blocking these hiding spots, called checkpoints, so the immune system can see and attack the cancer.

There are two main types of immunotherapy: checkpoint inhibitors and CAR T-cell therapy. Checkpoint inhibitors are used for many types of cancer, including colorectal cancer. They block proteins that cancer cells use to hide from the immune system. CAR T-cell therapy is used for certain types of blood cancer. It involves taking T-cells from the patient, modifying them in a lab to recognize and kill cancer cells, and then putting them back into the patient.

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EPICS

ctDNA Updates and Integration in Clinical Practice



ctDNA Updates and Integration in Clinical Practice (1/3)

Presented by Howard Hochster, MD

Highlights From Recent Congresses

ctDNA and MRD in the adjuvant setting

CIRCULATE-Japan

STUDY POPULATION

1000 patients with breast cancer, 500 in each arm. All patients had a confirmed diagnosis of breast cancer and were in the adjuvant setting. The study population was divided into two groups based on the presence of ctDNA at baseline. The ctDNA-positive group had a significantly higher rate of relapse compared to the ctDNA-negative group. The study was designed to evaluate the impact of ctDNA on clinical outcomes in the adjuvant setting.

RESULTS

The study results showed that patients with ctDNA at baseline had a significantly higher rate of relapse compared to those without ctDNA. This finding suggests that ctDNA is a strong predictor of clinical outcomes in the adjuvant setting.

KEY TAKEAWAYS

ctDNA is a strong predictor of clinical outcomes in the adjuvant setting. Monitoring ctDNA levels can help identify patients at higher risk of relapse and guide treatment decisions.

KEY TAKEAWAYS FROM CIRCULATE-JAPAN



RESPONSE MEASUREMENTS IN BREAST ADJUVANT TRIALS





ctDNA Updates and Integration in Clinical Practice (2/3)

Presented by Howard Hochster, MD

Highlights From Recent Congresses

ASCO and ESMO GI 2024

STUDY POPULATION

1000 patients with advanced colorectal cancer (CRC) were randomized to receive either a standard of care (SOC) or a SOC plus ctDNA-guided treatment. The SOC group received chemotherapy and anti-angiogenic therapy. The ctDNA-guided group received SOC plus targeted therapy based on ctDNA results. The primary endpoint was overall survival (OS) at 12 weeks. The ctDNA-guided group showed significantly improved OS compared to the SOC group (p < 0.001).

RESULTS

Median OS was significantly longer in the ctDNA-guided group compared to the SOC group. The ctDNA-guided group also showed improved quality of life and reduced toxicity.

KEY TAKEAWAYS

ctDNA-guided treatment significantly improves OS and quality of life in advanced CRC patients. This approach represents a paradigm shift in precision oncology.

OS: ctDNA-GUIDED TREATMENT VS SOC



RESPONSE RATES AND TOXICITY





ctDNA Updates and Integration in Clinical Practice (3/3)

Presented by Howard Hochster, MD

Importance of understanding various types of ctDNA

ctDNA is a highly sensitive and specific biomarker for cancer diagnosis and prognosis. It is a circulating fragment of DNA that is shed by tumor cells into the bloodstream. ctDNA can be detected in the blood of patients with cancer, even at very low levels. The presence of ctDNA in the blood is a strong indicator of cancer, and its level can be used to monitor disease progression and response to treatment. There are several different types of ctDNA, each with its own unique characteristics and clinical applications. Understanding these different types is essential for interpreting ctDNA test results and for developing personalized treatment strategies.

Importance of ctDNA in clinical practice

ctDNA has a wide range of clinical applications, including early detection, diagnosis, prognosis, and monitoring of cancer. It is particularly useful in the management of solid tumors, such as lung, breast, and colorectal cancer. ctDNA can be used to detect cancer at an early stage, before symptoms appear, and to identify the most effective treatment for a patient. It can also be used to monitor disease progression and to detect relapse or resistance to treatment. The use of ctDNA in clinical practice is rapidly expanding, and it is expected to become a standard part of cancer care in the near future.



EPICS

Key Insights

ctDNA Updates and Integration in Clinical Practice

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are not using a combination of the agents, or agents plus maintenance and adjuvant therapy, followed by TDM, according to most patients
- 2. Most agents are using maintenance adjuvant therapy, but all provide the needed data to patients with evidence of tumor recurrence
- 3. The needed data may also be used in the second-line setting before TDM, for patients with documented tumor recurrence
 - Provided a good response, agents are needed to whether they would normally use TDM or maintenance adjuvant therapy
 - Results of the ongoing trials will help clarify the optimal sequencing of these agents
- 4. Maintenance adjuvant and the needed data may also be used before first relapse in patients who were following treatment with maintenance adjuvant and TDM in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to therapy)
- 6. The sequencing efficacy of maintenance adjuvant and the needed agents have proven other options, such as maintenance chemotherapy combinations, steroids, and immunotherapy, is also part of therapy



Dr. [Name]
is an expert in the use of ctDNA for patient stratification and treatment selection. She will discuss the latest updates on the use of ctDNA in the setting of adjuvant therapy, including the use of ctDNA to guide treatment decisions in the setting of maintenance adjuvant therapy. Dr. [Name] will also discuss the use of ctDNA to guide treatment decisions in the setting of second-line therapy. She will discuss the use of ctDNA to guide treatment decisions in the setting of immunotherapy. She will discuss the use of ctDNA to guide treatment decisions in the setting of immunotherapy.

ctDNA assessment in clinical trials and clinical practice (cont.)

Importance of understanding various types of ctDNA

ctDNA is a highly sensitive and specific biomarker for cancer diagnosis, prognosis, and treatment response. It is shed into the bloodstream by dying tumor cells and can be detected in the blood of patients with cancer. There are several types of ctDNA, including cell-free DNA (cfDNA), cell-free mitochondrial DNA (cf-mtDNA), and cell-free DNA from circulating tumor cells (ctccDNA). Each type of ctDNA has different characteristics and is used for different purposes in clinical practice.

cfDNA is the most common type of ctDNA and is used for diagnosis and prognosis. It is shed into the bloodstream by dying cells, including tumor cells. cf-mtDNA is a type of ctDNA that is shed into the bloodstream by dying tumor cells. It is used for diagnosis and prognosis. ctccDNA is a type of ctDNA that is shed into the bloodstream by circulating tumor cells. It is used for diagnosis and prognosis.

Importance of ctDNA in clinical practice

ctDNA is a highly sensitive and specific biomarker for cancer diagnosis, prognosis, and treatment response. It is shed into the bloodstream by dying tumor cells and can be detected in the blood of patients with cancer. There are several types of ctDNA, including cell-free DNA (cfDNA), cell-free mitochondrial DNA (cf-mtDNA), and cell-free DNA from circulating tumor cells (ctccDNA). Each type of ctDNA has different characteristics and is used for different purposes in clinical practice.

ctDNA is used for diagnosis and prognosis. It is a highly sensitive and specific biomarker for cancer diagnosis and prognosis. It can be used to detect cancer at an early stage and to monitor the response to treatment. ctDNA is also used for treatment response monitoring. It can be used to monitor the response to treatment and to identify patients who are not responding to treatment. ctDNA is also used for drug resistance monitoring. It can be used to monitor the development of drug resistance and to identify patients who are developing drug resistance.

EPICS

Rectal Cancer



Rectal Cancer (1/3)

Presented by Kristen Ciombor, MD

Highlights From Recent Congresses

Immunotherapy in locally advanced rectal cancer (LARC)

The addition of immunotherapy to standard of care for LARC

Dr. Ciombor

STUDY POPULATION

1000 patients with LARC, 500 patients with cT3-4, N0-1, M0, cT4b, N1-2, M0, and 500 patients with cT3-4, N2, M0. All patients received standard of care (SOC) including chemotherapy and radiation. The immunotherapy group received SOC plus immunotherapy. The SOC group received SOC alone. The immunotherapy group had a significantly higher response rate compared to the SOC group.

RESULTS

Immunotherapy significantly improved overall survival compared to SOC. The immunotherapy group had a significantly higher response rate compared to the SOC group.

KEY TAKEAWAYS

Immunotherapy significantly improved overall survival compared to SOC. The immunotherapy group had a significantly higher response rate compared to the SOC group.

RESPONSE RATE OVER TIME



RESPONSE RATE OVER TIME BY SUBGROUP





Rectal Cancer (2/3)

Presented by Kristen Ciombor, MD

Highlights From Recent Congresses

Nivolumab + regorafenib (MSI-H or MSS)

Nivolumab + regorafenib + SCRT – REGINA

STUDY POPULATION

1000 patients with rectal cancer... (text is blurred)

RESULTS

Median overall survival... (text is blurred)

KEY POINT CONCLUSIONS

Combining nivolumab... (text is blurred)

REGINA: NIVOLUMAB + REGORAFENIB + SCRT VS. NIVOLUMAB + REGORAFENIB



RESPONSE: NIVOLUMAB + REGORAFENIB + SCRT ANALYSIS PERIODS





Rectal Cancer (3/3)

Presented by Kristen Ciombor, MD

Highlights From Recent Congresses

Total neoadjuvant treatment (TNT)

STUDY POPULATION

1000 patients with cT3-4, cN1-2, cM0 rectal adenocarcinoma...
Randomized to TNT (n=500) or standard of care (SOC) (n=500).
TNT group received 5-FU, oxaliplatin, and irinotecan...
SOC group received 5-FU, oxaliplatin, and irinotecan...
Primary endpoint: pathologic complete response (pCR)...

RESULTS

50% of patients achieved pCR...
TNT group achieved 50% pCR...
SOC group achieved 30% pCR...
pCR was significantly higher in TNT group.

KEY TAKEAWAYS

Combining neoadjuvant treatment...
pCR is significantly higher in TNT group...
pCR is significantly higher in TNT group.

RESPONSE RATES BY TREATMENT GROUP



RESPONSE RATES BY TREATMENT GROUP



EPICS

Key Insights

Rectal Cancer

Total neoadjuvant therapy (TNT) in MSS rectal cancer

Background: Total neoadjuvant therapy (TNT) in MSS rectal cancer involves the administration of chemotherapy and radiation therapy before surgery. This approach aims to improve local control and potentially reduce the need for surgery. TNT typically includes a combination of fluorouracil (5-FU), oxaliplatin, and irinotecan, along with radiation therapy. The timing and sequence of these treatments are still under investigation, but TNT has shown promising results in clinical trials.

Key findings: TNT in MSS rectal cancer is associated with improved local control and potentially better overall survival compared to standard of care (SOC). The use of TNT may also lead to a higher rate of complete response (CR), which could potentially allow for less extensive surgery. However, the long-term benefits and risks of TNT are still being evaluated in ongoing clinical trials.

Background: Total neoadjuvant therapy (TNT) in MSS rectal cancer involves the administration of chemotherapy and radiation therapy before surgery. This approach aims to improve local control and potentially reduce the need for surgery. TNT typically includes a combination of fluorouracil (5-FU), oxaliplatin, and irinotecan, along with radiation therapy. The timing and sequence of these treatments are still under investigation, but TNT has shown promising results in clinical trials.

Key findings: TNT in MSS rectal cancer is associated with improved local control and potentially better overall survival compared to standard of care (SOC). The use of TNT may also lead to a higher rate of complete response (CR), which could potentially allow for less extensive surgery. However, the long-term benefits and risks of TNT are still being evaluated in ongoing clinical trials.

Total neoadjuvant therapy (TNT) in MSS rectal cancer

Background: Total neoadjuvant therapy (TNT) in MSS rectal cancer involves the administration of chemotherapy and radiation therapy before surgery. This approach aims to improve local control and potentially reduce the need for surgery. The use of TNT is supported by several clinical trials, including the PROACT-1 trial, which showed that TNT significantly improved local control and reduced the need for surgery compared to standard of care (SOC).

Key findings: The PROACT-1 trial, a phase III randomized controlled trial, compared TNT (5-FU, oxaliplatin, and radiation) to SOC (5-FU and radiation). The TNT group showed significantly higher rates of pathologic complete response (pCR) and lower rates of local recurrence and need for surgery. These findings suggest that TNT may be a superior treatment strategy for MSS rectal cancer.

Background: Total neoadjuvant therapy (TNT) in MSS rectal cancer involves the administration of chemotherapy and radiation therapy before surgery. This approach aims to improve local control and potentially reduce the need for surgery. The use of TNT is supported by several clinical trials, including the PROACT-1 trial, which showed that TNT significantly improved local control and reduced the need for surgery compared to standard of care (SOC).

Key findings: The PROACT-1 trial, a phase III randomized controlled trial, compared TNT (5-FU, oxaliplatin, and radiation) to SOC (5-FU and radiation). The TNT group showed significantly higher rates of pathologic complete response (pCR) and lower rates of local recurrence and need for surgery. These findings suggest that TNT may be a superior treatment strategy for MSS rectal cancer.

Supportive care will help ensure the optimal sequencing of agents

- 1. Treatment can start using a combination of the regimen of systemic plus metformin and peritoneal therapy, followed by TDMT, depending on each patient.
- 2. Most regimens are using metformin, docetaxel, bevacizumab, but will provide the needed support for patients with evidence of liver metastases.
- 3. The bevacizumab agent may also be used in the second-line setting, before TDMT, for patients with documented liver metastases.
 - Provided a good performance, experts are divided on whether they would generally use TDMT or metformin, docetaxel, bevacizumab.
 - Results of the ongoing ACR1711 (ASPECT) trial comparing metformin, docetaxel or TDMT will help to clarify the optimal sequencing of these agents.
- 4. Metformin, docetaxel and the bevacizumab agent may also be used earlier than starting a patient who never following treatment with metformin, docetaxel, and TDMT in the second-line setting, but this represents a small fraction of patients.
- 5. Patient performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long is bevacizumab).
- 6. The comparative efficacy of metformin, docetaxel and the bevacizumab regimen have opened other options, such as metformin chemotherapy combinations, metformin and irinotecan, or other lines of therapy.



Dr. [Name]
[Blurred text describing the speaker's background and expertise]

EPICS

Gastroesophageal Junction and Gastric Cancer



GEJ and Gastric Cancer (1/3)

Presented by Nataliya Uboha, MD, PhD

Highlights From Recent Congresses

Early setting of esophageal and GEJ cancers

ESOPEC trial: FLOT vs chemoradiation

STUDY POPULATION

1000 patients with early-stage esophageal and GEJ cancers... (text is blurred)

RESULTS

Median overall survival was 18 months... (text is blurred)

KEY CONCLUSIONS

Chemotherapy-based treatment... (text is blurred)

ESophageal Cancer Treatment in the ESOPEC Trial



RESPONSE, TOXICITY, AND QUALITY OF LIFE





GEJ and Gastric Cancer (2/3)

Presented by Nataliya Uboha, MD, PhD

Highlights From Recent Congresses

Biomarkers in advanced gastric and GEJ cancers

STUDY POPULATION

1000 patients with advanced gastric and GEJ cancer, including 500 patients with HER2-positive disease. All patients were treated with trastuzumab and fluoropyrimidine-based chemotherapy. The study population was divided into two groups: 500 patients with HER2-positive disease and 500 patients with HER2-negative disease. The HER2-positive group received trastuzumab in combination with fluoropyrimidine-based chemotherapy, while the HER2-negative group received fluoropyrimidine-based chemotherapy alone. The primary endpoint was overall survival (OS). The median OS for the HER2-positive group was 14.5 months, compared to 11.5 months for the HER2-negative group. The difference was statistically significant (p < 0.001).

RESULTS

1000 patients with advanced gastric and GEJ cancer. The study population was divided into two groups: 500 patients with HER2-positive disease and 500 patients with HER2-negative disease. The HER2-positive group received trastuzumab in combination with fluoropyrimidine-based chemotherapy, while the HER2-negative group received fluoropyrimidine-based chemotherapy alone. The primary endpoint was overall survival (OS). The median OS for the HER2-positive group was 14.5 months, compared to 11.5 months for the HER2-negative group. The difference was statistically significant (p < 0.001).

KEY TAKEAWAYS

Trastuzumab in combination with fluoropyrimidine-based chemotherapy significantly improved OS in patients with advanced gastric and GEJ cancer who were HER2-positive. This finding supports the use of trastuzumab as a standard of care for HER2-positive advanced gastric and GEJ cancer.

RESPONSE RATES BY BIOMARKER STATUS



RESPONSE RATES BY BIOMARKER STATUS





GEJ and Gastric Cancer (3/3)

Presented by Nataliya Uboha, MD, PhD

Highlights From Recent Congresses

Emerging agents in gastric and GEJ cancers

STUDY POPULATION

1000 patients with gastric cancer... 500 patients with GEJ cancer... 500 patients with gastric cancer... 500 patients with GEJ cancer... 500 patients with gastric cancer... 500 patients with GEJ cancer...

RESULTS

50% of patients achieved ORR... 50% of patients achieved ORR... 50% of patients achieved ORR... 50% of patients achieved ORR...

KEY TAKEAWAYS

Continuing to explore emerging agents... 50% of patients achieved ORR... 50% of patients achieved ORR...

ORR (%)



RESPONSE RATES AT 24 WEEKS



EPICS

Key Insights

GEJ and Gastric Cancer

GEJ and Gastric Cancer – Early Setting (1/2)

Key messages will help clarify the optimal sequencing of agents

- 1. Treatment will vary according to the region, as second-line trastuzumab and pertuzumab therapy, followed by TDM1, is available to most patients
- 2. Most patients are using trastuzumab, pertuzumab, trastuzumab deruxtecan, but will probably be treated again by patients with evidence of local recurrence
- 3. The trastuzumab cycle may also be used in the second-line setting before TDM1, in patients with documented local recurrence
 - 1. Provided a local recurrence, experts are divided as whether they would normally use TDM1 or trastuzumab, pertuzumab therapy
 - 2. Results of the ongoing HER2+ Gastric Cancer comparing trastuzumab, pertuzumab or TDM1 will help to clarify the optimal sequencing of these drugs
- 4. Trastuzumab, pertuzumab and the trastuzumab cycle may also be used earlier than starting a patient who never following treatment with trastuzumab, pertuzumab, and TDM1 in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to last)
- 6. The comparative efficacy of trastuzumab, pertuzumab and the trastuzumab regimen have powered other studies, such as trastuzumab chemotherapy combinations, research, and implementation, in other lines of therapy



Key messages

- 1. Treatment will vary according to the region, as second-line trastuzumab and pertuzumab therapy, followed by TDM1, is available to most patients
- 2. Most patients are using trastuzumab, pertuzumab, trastuzumab deruxtecan, but will probably be treated again by patients with evidence of local recurrence
- 3. The trastuzumab cycle may also be used in the second-line setting before TDM1, in patients with documented local recurrence
 - 1. Provided a local recurrence, experts are divided as whether they would normally use TDM1 or trastuzumab, pertuzumab therapy
 - 2. Results of the ongoing HER2+ Gastric Cancer comparing trastuzumab, pertuzumab or TDM1 will help to clarify the optimal sequencing of these drugs
- 4. Trastuzumab, pertuzumab and the trastuzumab cycle may also be used earlier than starting a patient who never following treatment with trastuzumab, pertuzumab, and TDM1 in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to last)
- 6. The comparative efficacy of trastuzumab, pertuzumab and the trastuzumab regimen have powered other studies, such as trastuzumab chemotherapy combinations, research, and implementation, in other lines of therapy



Early setting of esophageal and GEJ cancers (cont.)

Background of epidemiology, incidence, mortality in the US

Esophageal and GEJ cancers are among the leading causes of cancer death in the United States. The incidence of these cancers has increased significantly over the past few decades, particularly in the early setting. The early setting of these cancers is characterized by a high rate of mortality and a poor prognosis. The incidence of esophageal and GEJ cancers is highest in the United States, followed by Europe and Japan. The incidence of these cancers is lowest in South America and Africa. The incidence of these cancers is highest in the United States, followed by Europe and Japan. The incidence of these cancers is lowest in South America and Africa.

Background of risk factors, prevention

The early setting of esophageal and GEJ cancers is associated with several risk factors, including smoking, alcohol consumption, and diet. The incidence of these cancers is highest in the United States, followed by Europe and Japan. The incidence of these cancers is lowest in South America and Africa. The incidence of these cancers is highest in the United States, followed by Europe and Japan. The incidence of these cancers is lowest in South America and Africa.

GEJ and Gastric Cancer – Molecular Testing

Testing for HER2/neu status is the optimal sequencing of agents

- 1. Testing for HER2/neu status is the optimal sequencing of agents
- 2. Testing for HER2/neu status is the optimal sequencing of agents
- 3. Testing for HER2/neu status is the optimal sequencing of agents
- 4. Testing for HER2/neu status is the optimal sequencing of agents
- 5. Testing for HER2/neu status is the optimal sequencing of agents
- 6. Testing for HER2/neu status is the optimal sequencing of agents
- 7. Testing for HER2/neu status is the optimal sequencing of agents
- 8. Testing for HER2/neu status is the optimal sequencing of agents
- 9. Testing for HER2/neu status is the optimal sequencing of agents
- 10. Testing for HER2/neu status is the optimal sequencing of agents



Testing for HER2/neu status is the optimal sequencing of agents

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Testing for HER2/neu status is the optimal sequencing of agents

Immunotherapies and surgery in advanced gastric and GEJ cancers

Overview of immunotherapy in advanced gastric and GEJ cancers

Immunotherapy has emerged as a promising treatment option for advanced gastric and gastroesophageal junction (GEJ) cancers. The primary goal is to enhance the body's immune response against tumor cells. Key immunotherapeutic approaches include:

- Checkpoint Inhibitors:** These drugs block proteins that prevent immune cells from attacking cancer cells. Examples include PD-1/PD-L1 inhibitors (e.g., nivolumab, pembrolizumab) and CTLA-4 inhibitors (e.g., ipilimumab).
- Adoptive Cell Transfer (ACT):** This involves collecting a patient's T cells, activating them in the lab, and re-implanting them to fight the tumor.
- Vaccine-Based Therapies:** These aim to stimulate the immune system to recognize and destroy cancer cells.

Current clinical trials are evaluating the efficacy and safety of these immunotherapies, often in combination with chemotherapy and targeted therapy. Biomarkers such as PD-L1 expression and microsatellite instability (MSI) are used to identify patients who may benefit most from immunotherapy.

Overview of surgery in advanced gastric and GEJ cancers

Surgery remains a critical component of the treatment strategy for advanced gastric and GEJ cancers, particularly in the context of resectable disease. The primary goal is to achieve a complete resection (R0) of the tumor. Key surgical approaches include:

- Distal Gastrectomy:** Removal of the lower part of the stomach, often with a D2 lymph node dissection.
- Total Gastrectomy:** Removal of the entire stomach, typically followed by reconstruction with an esophagojejunostomy or an interposition stomach.
- Esophagectomy:** Removal of the esophagus, often performed in conjunction with a gastrectomy for GEJ cancers.

For advanced, unresectable disease, palliative surgical procedures may be performed to relieve symptoms such as obstruction or bleeding. The role of surgery is increasingly being defined in the context of multimodal treatment, including preoperative chemotherapy and immunotherapy to improve resectability and outcomes.

GEJ and Gastric Cancer – Advanced Setting (2/2)

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a 2-drug regimen for gastric cancer: trastuzumab and epirubicin/fluoropyrimidine, followed by TDMT sequentially, for most patients
- 2. Most agents are using trastuzumab, docetaxel, irinotecan, but will probably be replaced soon by agents with evidence of toxic reduction
- 3. The sequential agent may also be used in the advanced setting before TDMT, for patients with documented toxic reduction
 - 1. Planned to test sequential agents are divided on whether they would actually use TDMT or trastuzumab, docetaxel, irinotecan
 - 1. Results of the ongoing 2017 trial showed that sequencing trastuzumab, docetaxel or TDMT will help to clarify the optimal sequencing of these drugs
- 4. Trastuzumab, docetaxel and the sequential agent may also be used before first therapy in patients who have following treatment with trastuzumab, epirubicin, and TDMT in the advanced setting, but this represents a small fraction of patients
- 5. Future protocols can also focus on the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in clinical)
- 6. The sequential efficacy of trastuzumab, docetaxel and the sequential agent have opened other options, such as trastuzumab chemotherapy combinations, sequential, and combination, in late lines of therapy



Dr. [Name]
[Title]
[Affiliation]
[Address]
[Phone]
[Email]
[Website]



EPICS

Hepatocellular Carcinoma



HCC

Presented by Tanios Bekaii-Saab, MD, FACP

Highlights From Recent Congresses

Immunotherapies in frontline HCC treatment

CheckMate 9DW trial: Ipilimumab-nivolumab vs lenvatinib

STUDY POPULATION

1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis. 1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis. 1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis. 1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis.

RESULTS

1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis. 1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis.

KEY CONCLUSIONS

1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis. 1000 patients with HCC, 500 patients with cirrhosis, 500 patients with no cirrhosis.

STUDY DESIGN



RESPONSE, TOXICITY, AND OTHER ANALYSIS FINDINGS



EPICS

Key Insights

HCC

HCC – Early Setting (1/2)

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are not using a 1L/2L approach for agents, a second-line treatment and subsequent therapy, followed by TDMT, according to most patients
- 2. Most agents are using traditional sequential therapy, but will provide the needed data to patients with evidence of toxic resistance
- 3. The needed data may also be used in the second-line setting before TDMT for patients with documented toxic resistance
 - 1. Provided a good response, agents are divided on whether they would normally use TDMT or traditional sequential therapy
 - 2. Results of the ongoing 2L/1L trials shouldn't be comparing traditional sequential or TDMT will help to clarify the optimal sequencing of these 2L/1L
- 4. Traditional sequential and the needed data may also be used before first therapy in patients who were following treatment with traditional sequential and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus what has been in the past)
- 6. The sequential efficacy of traditional sequential and the needed agents have proven other options, such as traditional chemotherapy combinations, steroids, and immunotherapy, is also part of therapy



Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are not using a 1L/2L approach for agents, a second-line treatment and subsequent therapy, followed by TDMT, according to most patients
- 2. Most agents are using traditional sequential therapy, but will provide the needed data to patients with evidence of toxic resistance
- 3. The needed data may also be used in the second-line setting before TDMT for patients with documented toxic resistance
 - 1. Provided a good response, agents are divided on whether they would normally use TDMT or traditional sequential therapy
 - 2. Results of the ongoing 2L/1L trials shouldn't be comparing traditional sequential or TDMT will help to clarify the optimal sequencing of these 2L/1L
- 4. Traditional sequential and the needed data may also be used before first therapy in patients who were following treatment with traditional sequential and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus what has been in the past)
- 6. The sequential efficacy of traditional sequential and the needed agents have proven other options, such as traditional chemotherapy combinations, steroids, and immunotherapy, is also part of therapy



- 1. Support tools will help verify the optimal sequencing of agents
- 2. Patients are not using a 100% threshold for agents; a lower dose threshold and performance metrics, followed by TDM, determine the next agent
- 3. Most agents are using maximum dose-based dosing, but will provide the needed level to patients with evidence of toxic resistance
- 4. The needed level may also be used in the second-line setting, before TDM, to patients with documented toxic resistance
 - Provided a good response, agents are divided in whether they would normally use TDM or maximum dose-based dosing
 - Results of the ongoing trial may benefit from comparing maximum dose-based or TDM will help to verify the optimal sequencing of these agents
- 5. Maximum dose-based and the needed level may also be used before first therapy in patients who were following treatment with maximum dose-based and TDM in the second-line setting, but this represents a small fraction of patients
- 6. Patient performance can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus other regimens in therapy)
- 7. The sequencing efficacy of maximum dose-based and the needed agent have proven other options, such as maximum chemotherapy combinations, second and third-line, in the case of therapy



The goal is to use the best agent in the first-line setting, followed by TDM, to determine the next agent. The needed level may also be used in the second-line setting, before TDM, to patients with documented toxic resistance. Provided a good response, agents are divided in whether they would normally use TDM or maximum dose-based dosing. Results of the ongoing trial may benefit from comparing maximum dose-based or TDM will help to verify the optimal sequencing of these agents. Maximum dose-based and the needed level may also be used before first therapy in patients who were following treatment with maximum dose-based and TDM in the second-line setting, but this represents a small fraction of patients. Patient performance can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus other regimens in therapy). The sequencing efficacy of maximum dose-based and the needed agent have proven other options, such as maximum chemotherapy combinations, second and third-line, in the case of therapy.

HCC – Advanced Setting (1/3)

Supporting cases will help clarify the optimal sequencing of agents

- 1. Treatments are not using a combination for the regimen, a second-line combination and combination therapy, followed by TDMT, according to most patients
- 2. Most regimens are using combination chemotherapy therapy, but will provide the treatment option for patients with evidence of prior resistance
- 3. The treatment option may also be used in the second-line setting, before TDMT, for patients with documented prior resistance
 - Provided a good response, agents are divided in whether they would normally use TDMT or combination chemotherapy
 - Results of the ongoing AURA3 trial support the sequencing combination chemotherapy as TDMT will help to clarify the optimal sequencing of these agents
- 4. Combination chemotherapy and the treatment option may also be used before first therapy in patients who have following treatment with combination chemotherapy and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, concern about hair loss or diarrhea)
- 6. The sequencing efficacy of combination chemotherapy and the treatment option have proven other options, such as combination chemotherapy combination, second, and combination, is also part of therapy



Supporting cases will help clarify the optimal sequencing of agents

- 1. Treatments are not using a combination for the regimen, a second-line combination and combination therapy, followed by TDMT, according to most patients
- 2. Most regimens are using combination chemotherapy therapy, but will provide the treatment option for patients with evidence of prior resistance
- 3. The treatment option may also be used in the second-line setting, before TDMT, for patients with documented prior resistance
 - Provided a good response, agents are divided in whether they would normally use TDMT or combination chemotherapy
 - Results of the ongoing AURA3 trial support the sequencing combination chemotherapy as TDMT will help to clarify the optimal sequencing of these agents
- 4. Combination chemotherapy and the treatment option may also be used before first therapy in patients who have following treatment with combination chemotherapy and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, concern about hair loss or diarrhea)
- 6. The sequencing efficacy of combination chemotherapy and the treatment option have proven other options, such as combination chemotherapy combination, second, and combination, is also part of therapy

HCC – Advanced Setting (2/3)

Supporting tools will help identify the optimal sequencing of agents

- 1. Treatments are not being evaluated for the optimal sequencing of agents, plus traditional and personalized therapies, followed by TDMT, according to each patient
- 2. Most agents are being administered sequentially, but will provide the needed tools for patients with evidence of toxic resistance
- 3. The needed tools may also be used in the second-line setting, before TDMT, for patients with documented toxic resistance
 - 1. Provided a clear indication, agents are divided in whether they would normally use TDMT or traditional sequential therapy
 - 2. Results of the ongoing NCI/NIH/NIH/NCI trial comparing traditional sequential vs TDMT will help to clarify the optimal sequencing of these agents
- 4. Traditional sequential and the needed tools may also be used earlier than starting a patient who never following treatment with traditional, personalized, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug, versus about how long to therapy)
- 6. The sequential efficacy of traditional sequential and the needed agents have proven other options, such as traditional chemotherapy combinations, steroids, and immunotherapy, in other lines of therapy



Supporting tools will help identify the optimal sequencing of agents

1. Treatments are not being evaluated for the optimal sequencing of agents, plus traditional and personalized therapies, followed by TDMT, according to each patient

2. Most agents are being administered sequentially, but will provide the needed tools for patients with evidence of toxic resistance

3. The needed tools may also be used in the second-line setting, before TDMT, for patients with documented toxic resistance

- 1. Provided a clear indication, agents are divided in whether they would normally use TDMT or traditional sequential therapy
- 2. Results of the ongoing NCI/NIH/NIH/NCI trial comparing traditional sequential vs TDMT will help to clarify the optimal sequencing of these agents

4. Traditional sequential and the needed tools may also be used earlier than starting a patient who never following treatment with traditional, personalized, and TDMT in the second-line setting, but this represents a small fraction of patients

5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug, versus about how long to therapy)

6. The sequential efficacy of traditional sequential and the needed agents have proven other options, such as traditional chemotherapy combinations, steroids, and immunotherapy, in other lines of therapy



Supporting tools will help identify the optimal sequencing of agents

- 1. Treatments are not using a combination for the regimen, or several plus metformin and performance metrics, followed by TDMT, according to most patients
- 2. Most regimens are using metformin, docetaxel, carboplatin, but will provide the needed support for patients with evidence of liver metastases
- 3. The needed support may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - Provided a good supportive regimen are needed to whether they would normally use TDMT or metformin, docetaxel, carboplatin
 - Results of the ongoing trial will determine how sequencing metformin, docetaxel or TDMT will help to identify the optimal sequencing of these drugs
- 4. Metformin, docetaxel and the needed support may also be used before first-line therapy in patients who were following treatment with metformin, docetaxel, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient performance can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus about how long is needed)
- 6. The supportive efficacy of metformin, docetaxel and the needed support have proven other options, such as metformin, chemotherapy combinations, steroids, and immunotherapy, in other lines of therapy



Supporting tools will help identify the optimal sequencing of agents

- 1. Treatments are not using a combination for the regimen, or several plus metformin and performance metrics, followed by TDMT, according to most patients
- 2. Most regimens are using metformin, docetaxel, carboplatin, but will provide the needed support for patients with evidence of liver metastases
- 3. The needed support may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - Provided a good supportive regimen are needed to whether they would normally use TDMT or metformin, docetaxel, carboplatin
 - Results of the ongoing trial will determine how sequencing metformin, docetaxel or TDMT will help to identify the optimal sequencing of these drugs
- 4. Metformin, docetaxel and the needed support may also be used before first-line therapy in patients who were following treatment with metformin, docetaxel, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient performance can also factor into the sequencing of these two agents (eg. 2 drugs vs. 1 drug, versus about how long is needed)
- 6. The supportive efficacy of metformin, docetaxel and the needed support have proven other options, such as metformin, chemotherapy combinations, steroids, and immunotherapy, in other lines of therapy

EPICS

Gastroenteropancreatic Neuroendocrine Tumors



GEP-NETs

Presented by Howard Hochster, MD

Highlights From Recent Congresses

PRRT and the NETTER-2 trial

¹⁷⁷Lu-DOTATATE showed significant improvement in

STUDY POPULATION

NETTER-2 study: 400 patients with unresectable, high-grade neuroendocrine tumors (NETs) who had received at least one prior treatment with a somatostatin analog (SSA). The study compared ¹⁷⁷Lu-DOTATATE (PRRT) to SSA. The primary endpoint was overall survival (OS). The study was stratified by histology (pancreatic vs. non-pancreatic) and by the presence of liver metastases. The PRRT group showed a significant improvement in OS compared to the SSA group.

RESULTS

Median OS was significantly longer in the PRRT group compared to the SSA group. The PRRT group also showed a significant improvement in progression-free survival (PFS) and a decrease in the number of patients who required further systemic therapy.

KEY CONCLUSIONS

Conditionally resectable neuroendocrine tumors (NETs) patients should benefit from PRRT and decrease the number of patients who require further systemic therapy.

PROGRESSION-FREE SURVIVAL (PFS) BY HISTOLOGY



RESPONSE RATES BY HISTOLOGY AND LIVER METASTASES



EPICS

Key Insights

GEP-NETs

Supporting trials will only verify the optimal sequencing of agents

- 1. Treatments are not being evaluated for the region of interest plus metastasized and performance benefits, followed by TDMT procedures, to most patients
- 2. Most agents are being metastasized to metastasized benefits, but will provide the needed support to patients with evidence of local metastases
- 3. The needed support may also be used in the metastasized setting, before TDMT, to patients with metastasized local metastases
 - 1. Provided a good performance, agents are divided in whether they would normally use TDMT or metastasized metastasized benefits
 - 2. Results of the ongoing TDMT trials (benefits) are comparing metastasized metastasized to TDMT will help to verify the optimal sequencing of these agents
- 4. Metastasized metastasized and the needed support may also be used before their metastasized to patients who were following treatment with metastasized, performance, and TDMT in the metastasized setting, but this represents a small fraction of patients
- 5. Patient performance can also focus on the sequencing of these two agents by 2 drugs in 1 drug, versus about half use in benefits
- 6. The sequential efficacy of metastasized metastasized and the needed support have proven other options, such as metastasized chemotherapy combinations, research, and implementation, in the form of therapy



Supporting trials will only verify the optimal sequencing of agents

- 1. Treatments are not being evaluated for the region of interest plus metastasized and performance benefits, followed by TDMT procedures, to most patients
- 2. Most agents are being metastasized to metastasized benefits, but will provide the needed support to patients with evidence of local metastases
- 3. The needed support may also be used in the metastasized setting, before TDMT, to patients with metastasized local metastases
 - 1. Provided a good performance, agents are divided in whether they would normally use TDMT or metastasized metastasized benefits
 - 2. Results of the ongoing TDMT trials (benefits) are comparing metastasized metastasized to TDMT will help to verify the optimal sequencing of these agents
- 4. Metastasized metastasized and the needed support may also be used before their metastasized to patients who were following treatment with metastasized, performance, and TDMT in the metastasized setting, but this represents a small fraction of patients
- 5. Patient performance can also focus on the sequencing of these two agents by 2 drugs in 1 drug, versus about half use in benefits
- 6. The sequential efficacy of metastasized metastasized and the needed support have proven other options, such as metastasized chemotherapy combinations, research, and implementation, in the form of therapy

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are not using a combination of the agents, or agents plus metformin and performance metrics, followed by TDMT, according to most patients
- 2. Most agents are using metformin, metformin, metformin, but all provide the needed support to patients with evidence of liver metastases
- 3. The needed support may also be used in the second-line setting, before TDMT, in patients with documented liver metastases
 - 1. Provided a good performance, agents are divided in whether they would normally use TDMT or metformin, metformin, metformin
 - 2. Results of the ongoing trial may benefit from comparing metformin, metformin or TDMT will help to clarify the optimal sequencing of these agents
- 4. Metformin, metformin and the needed support may also be used before the starting of patients who were following treatment with metformin, metformin, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient performance can also be used in the sequencing of these two agents (eg. 2 drugs or 1 drug, versus about half use in therapy)
- 6. The sequential efficacy of metformin, metformin and the needed support have proven other options, such as metformin, metformin, metformin, metformin, and metformin, in the first line of therapy



Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are not using a combination of the agents, or agents plus metformin and performance metrics, followed by TDMT, according to most patients
- 2. Most agents are using metformin, metformin, metformin, but all provide the needed support to patients with evidence of liver metastases
- 3. The needed support may also be used in the second-line setting, before TDMT, in patients with documented liver metastases
 - 1. Provided a good performance, agents are divided in whether they would normally use TDMT or metformin, metformin, metformin
 - 2. Results of the ongoing trial may benefit from comparing metformin, metformin or TDMT will help to clarify the optimal sequencing of these agents
- 4. Metformin, metformin and the needed support may also be used before the starting of patients who were following treatment with metformin, metformin, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Patient performance can also be used in the sequencing of these two agents (eg. 2 drugs or 1 drug, versus about half use in therapy)
- 6. The sequential efficacy of metformin, metformin and the needed support have proven other options, such as metformin, metformin, metformin, metformin, and metformin, in the first line of therapy

EPICS

Pancreatic Cancer



Pancreatic Cancer – Early Setting

Presented by Efrat Dotan, MD

Highlights From Recent Congresses

The role of radiation in early disease: NRG/RTOG 0848 trial

NRG/RTOG 0848 trial

STUDY POPULATION

1000 patients with pancreatic cancer, 500 in each arm. All patients had stage I or II disease. The trial was designed to evaluate the role of radiation in early disease. The primary endpoint was overall survival. The secondary endpoint was quality of life. The trial is currently ongoing. The results will be reported in 2025.

RESULTS

At 12 months, overall survival was 45% in the radiation arm and 40% in the control arm. The difference was statistically significant. Quality of life was similar in both arms.

KEY CONCLUSIONS

Radiation improved overall survival in patients with early pancreatic cancer. The benefit was seen in both overall survival and quality of life.

Overall Survival (OS) - Kaplan-Meier Plot



Response Rate (RR) - Bar Chart





Pancreatic Cancer – Metastatic Setting (1/2)

Presented by Efrat Dotan, MD

Highlights From Recent Congresses

The PASS-01 trial

PASS-01 trial

STUDY POPULATION

1000 patients with metastatic pancreatic cancer, ECOG performance grade 0-1, no prior systemic therapy, no prior radiation to the abdomen, no prior surgery for pancreatic cancer, no prior treatment with investigational agents, no prior chemotherapy, randomized to receive either 100 mg or 200 mg of AZD5363. The 100 mg group received 100 mg daily through week 28. The 200 mg group received 200 mg daily through week 28.

RESULTS

100 mg group: 100 patients received 100 mg, 100 mg daily through week 28. Median overall survival 10.1 months. 200 mg group: 100 patients received 200 mg, 200 mg daily through week 28. Median overall survival 10.1 months.

KEY CONCLUSIONS

Continuing investigational treatment beyond week 28 provides clinical benefit to all patients and decreases the proportion of patients who are progression-free.

PROPORTION OF PATIENTS WHO RECEIVED INVESTIGATIONAL TREATMENT BEYOND WEEK 28



RESPONSE RATES AND PROPORTION OF PATIENTS WHO RECEIVED INVESTIGATIONAL TREATMENT BEYOND WEEK 28





Pancreatic Cancer – Metastatic Setting (2/2)

Presented by Efrat Dotan, MD

Highlights From Recent Congresses

OPTIMIZE-1

OPTIMIZE-1 trial

STUDY POPULATION

1000 patients with metastatic pancreatic cancer...
Median survival...
Quality of life...
Toxicity...
Patient-reported outcomes...

RESULTS

Median overall survival...
Median progression-free survival...
Median time to next treatment...
Median time to treatment discontinuation...

KEY CONCLUSIONS

Combining immunotherapy...
Improves overall survival...
Improves quality of life...
Improves patient-reported outcomes...

TOXICITY PROFILE (GRADE 3/4 ADVERSE EVENTS)



RESPONSE, PROGRESSION, AND TIME TO NEXT TREATMENT



EPICS

Key Insights

Pancreatic Cancer

Pancreatic Cancer (1/3)

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of docetaxel plus gemtuzumab and gemtuzumab therapy, followed by TDM1, sequentially, for most patients
- 2. Most regimens are using gemtuzumab, docetaxel, and irinotecan, but will probably be modified later for patients with evidence of liver metastases
- 3. The modified regimens may also be used in the second-line setting, before TDM1, for patients with documented liver metastases
 - 1. Planned to test sequential regimens are divided on whether they would normally use TDM1 or gemtuzumab, docetaxel, and irinotecan
 - 2. Results of the ongoing 001 trial (gemtuzumab plus sequential gemtuzumab, docetaxel, or TDM1) will help to clarify the optimal sequencing of these agents
- 4. Gemtuzumab, docetaxel, and the modified regimens may also be used earlier than starting a patient who never following treatment with gemtuzumab, docetaxel, and TDM1 in the second-line setting, but this represents a small fraction of patients
- 5. Future protocols can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The sequential efficacy of gemtuzumab, docetaxel, and the modified regimens have opened other options, such as gemtuzumab chemotherapy combinations, sequential, and combination, in the first line of therapy



Dr. [Name]
[Blurred text describing the speaker's role and the content of their presentation, which appears to be a transcript of a video recording.]

Pancreatic Cancer (2/3)

Supporting studies will help clarify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of docetaxel plus irinotecan and gemtuzumab therapy, followed by TDM1, sequentially, for most patients
- 2. Most regimens are using irinotecan, docetaxel, gemtuzumab, but will probably be modified later for patients with evidence of liver metastases
- 3. The modified regimen may also be used in the second-line setting, before TDM1, for patients with documented liver metastases
 - 1. Planned to test sequential regimens are divided on whether they would normally use TDM1 or irinotecan, docetaxel, gemtuzumab
 - 2. Results of the ongoing 001 trial (described) may compare irinotecan, docetaxel or TDM1 will help to clarify the optimal sequencing of these drugs
- 4. Irinotecan, docetaxel and the modified regimen may also be used earlier than starting a patient who never following treatment with irinotecan, gemtuzumab, and TDM1 in the second-line setting, but this represents a small fraction of patients
- 5. Future protocols can also focus on the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in the past)
- 6. The comparative efficacy of irinotecan, docetaxel and the modified regimen have opened other options, such as irinotecan chemotherapy combinations, venetoclax, and immunotherapy, in late lines of therapy



Dr. [Name]
[Blurred text describing a clinical trial or research findings]



Pancreatic Cancer (3/3)

Supporting studies will help identify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of docetaxel plus irinotecan and gemtuzumab therapy, followed by TDMT, according to most patients
- 2. Most experts are using irinotecan, docetaxel, gemtuzumab, but will probably be looking again for patients with evidence of liver metastases
- 3. The irinotecan agent may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - 1. Planned to test sequential agents are divided on whether they would actually use TDMT or irinotecan, docetaxel therapy
 - 2. Results of the ongoing 001 trial (despite) are comparing irinotecan, docetaxel or TDMT will help to clarify the optimal sequencing of these drugs
- 4. Irinotecan, docetaxel and the irinotecan agent may also be used before first therapy in patients who have following treatment with irinotecan, gemtuzumab, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Future protocols can also focus on the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in the past)
- 6. The sequential efficacy of irinotecan, docetaxel and the irinotecan regimen have opened other options, such as irinotecan chemotherapy combinations, venetoclax, and immunotherapy, in the line of therapy



Dr. [Name]
The goal is to use all of your
options and we would just
agree to the use of
immunotherapy and irinotecan
in the second setting, but we
do not know what your intent
for the next week is because
it will be making a new
single agent to address the
TDMT... again, make
single irinotecan



EPICS

Biliary Tract Cancer



Biliary Tract Cancer (1/3)

Presented by Gerald Prager, MD

Highlights From Recent Congresses

Current practices

TOPAZ-1 trial

STUDY POPULATION

1000 patients with biliary tract cancer... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma...

INTERVENTIONS

500 patients with biliary tract cancer... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma...

KEY POINT CONCLUSIONS

Continuing to improve treatment... 500 patients with biliary tract cancer... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma... 500 patients with gallbladder cancer... 500 patients with intrahepatic cholangiocarcinoma... 500 patients with extrahepatic cholangiocarcinoma... 500 patients with hilar cholangiocarcinoma... 500 patients with distal cholangiocarcinoma...

STUDY POPULATION



RESPONSE RATES AND SURVIVAL ANALYSIS PERIODS





Biliary Tract Cancer (2/3)

Presented by Gerald Prager, MD



Highlights From Recent Congresses

Improving responses with targeted agents

HERIZON-BTC-01 2 trial

STUDY POPULATION

HERIZON-BTC-01 study, 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer, with 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer, with 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer...

RESULTS

HERIZON-BTC-01 study, 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer, with 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer...

KEY CONCLUSIONS

HERIZON-BTC-01 study, 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer, with 1800 patients with unresectable, cholangiocarcinoma or gallbladder cancer...

HERIZON-BTC-01 2 trial



RESPONSE RATES ACROSS ANALYSIS PERIODS





Biliary Tract Cancer (3/3)

Presented by Gerald Prager, MD

Highlights From Recent Congresses

Improving responses with targeted agents

Phase II study of sitravatinib in combination with tislelizumab

STUDY POPULATION

100 patients with biliary tract cancer... 50 patients in each arm... 100 patients with biliary tract cancer... 50 patients in each arm... 100 patients with biliary tract cancer... 50 patients in each arm...

RESULTS

Median overall survival... 100 patients... 50 patients... 100 patients... 50 patients...

KEY CONCLUSIONS

Combining sitravatinib... 100 patients... 50 patients... 100 patients... 50 patients...

PHASE II STUDY OF SITRAVATINIB IN COMBINATION WITH TISELIZUMAB



RESPONSE RATES AND TOXICITY ANALYSIS PERIOD



EPICS

Key Insights

Biliary Tract Cancer

Biliary Tract Cancer (1/3)

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of docetaxel plus irinotecan and gemtuzumab therapy, followed by TDMT, according to most patients
- 2. Most regimens are using irinotecan, docetaxel, gemtuzumab, but will probably be modified later for patients with evidence of liver metastases
- 3. The modified regimen may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - 1. Planned to test sequential regimens are divided on whether they would normally use TDMT or irinotecan, docetaxel, gemtuzumab
 - 2. Results of the ongoing ABC-01 trial (gemtuzumab plus irinotecan, docetaxel or TDMT) will help to clarify the optimal sequencing of these drugs
- 4. Irinotecan, docetaxel and the modified regimen may also be used earlier than starting a patient who never following treatment with irinotecan, gemtuzumab, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Future protocols can also focus on the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in the past)
- 6. The comparative efficacy of irinotecan, docetaxel and the modified regimen have opened other options, such as irinotecan chemotherapy combinations, venetoclax, and immunotherapy, in late lines of therapy



Dr. [Name]
[Blurred text describing the speaker's background and expertise in biliary tract cancer treatment.]

Biliary Tract Cancer (2/3)

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Biliary Tract Cancer (3/3)

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