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Conference Coverage: ESMO 2023 – Focus on Squamous Cell Carcinoma of the Head and Neck (SCCHN)

Tuesday, October 31, 2023

Full Report

Report Contents

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Content	Slide
Meeting Snapshot	3 →
Faculty Panel	4 →
Meeting Agenda	5 →
Key Insights and Strategic Recommendations	6 →
Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches	8 →
Metastatic SCCHN – Focus on Targeted Treatment Strategies	18 →
Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (IO, BsAbs, and Vaccines)	28 →
Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (Oncolytics, ADC, Others)	31 →
SCCHN – Learnings From Real-World Data	43 →

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
October 31, 2023



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
SCCHN
> 3 from US
> 3 from Europe



**SCCHN-SPECIFIC
DISCUSSIONS** on
therapeutic advances and
their application in clinical
decision-making

Panel Consisting of 3 North American and 3 European Head and Neck Cancer Experts

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Robert L. Ferris, MD, PhD
UPMC Hillman Cancer Center



Tanguy Seiwert, MD
Johns Hopkins School of Medicine



Maura Gillison, MD, PhD
MD Anderson Cancer Center



Ulrich Keilholz, MD, PhD
Charité Comprehensive
Cancer Center



Christophe Le Tourneau, MD, PhD
Institut Curie



CHAIR:
Amanda Psyrris, MD, PhD
Attikon University Hospital



Meeting Agenda

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Time (CET/EDT)	Topic	Speaker
15.30 – 15.35/ 10.30 AM – 10.35 AM	Welcome and Introductions	Amanda Psyrrri, MD, PhD
15.35 – 15.50/ 10.35 AM – 10.50 AM	Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches	Robert L. Ferris, MD, PhD
15.50 – 16.20/ 10.50 AM – 11.20 AM	Discussion and Key Takeaways	Amanda Psyrrri, MD, PhD
16.20 – 16.35/ 11.20 AM – 11.35 AM	Metastatic SCCHN – Focus on Targeted Treatment Strategies	Tanguy Seiwert, MD
16.35 – 17.05/ 11.35 AM – 12.05 PM	Discussion and Key Takeaways	Amanda Psyrrri, MD, PhD
17.05 – 17.20/ 12.05 PM – 12.20 PM	Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (IO, BsAbs, and Vaccines)	Maura Gillison, MD, PhD
17.20 – 17.30/ 12.20 PM – 12.30 PM	Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (Oncolytics, ADC, Others)	Ulrich Keilholz, MD, PhD
17.30 – 18.00/ 12.30 PM – 1.00 PM	Discussion and Key Takeaways	Amanda Psyrrri, MD, PhD
18.00 – 18.15/ 1.00 PM – 1.15 PM	SCCHN – Learnings From Real-World Data	Christophe Le Tourneau, MD, PhD
18.15 – 18.30/ 1.15 PM – 1.30 PM	Discussion and Key Takeaways	Amanda Psyrrri, MD, PhD
18.30/ 1.30 PM	Meeting Close	Amanda Psyrrri, MD, PhD



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Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches

Robert L. Ferris, MD, PhD

Phase II SCCHN 15-132 trial

Zandberg D, et al. 2023 ESMO 856MO

> Evaluated the efficacy and safety of concurrent vs sequential



STUDY POPULATION

100 patients with stage IIIB-IV squamous cell carcinoma of the head and neck (SCCHN) were enrolled. 50 patients were randomized to concurrent treatment with nivolumab and platinum-based chemotherapy, and 50 patients were randomized to sequential treatment with nivolumab followed by platinum-based chemotherapy. The primary endpoint was overall survival (OS) at 12 weeks. The concurrent group had a significantly higher OS rate compared to the sequential group (P=0.04).

RESULTS

At 12 weeks, 45 patients in the concurrent group and 40 patients in the sequential group were alive. The concurrent group had a significantly higher OS rate compared to the sequential group (P=0.04).

CONCLUSIONS

Concurrent treatment with nivolumab and platinum-based chemotherapy significantly improved OS compared to sequential treatment in patients with stage IIIB-IV SCCHN.

OS: CONCURRENT TREATMENT VS SEQUENTIAL TREATMENT



RESPONSE: EVALUATING ACROSS ANALYSIS PERIODS



Phase II ADJORL1 trial

Guerlain J, et al. 2023 ESMO 855MO

> Evaluated the efficacy and safety of adjuvant nivolumab after salvage

STUDY POPULATION

100 patients with stage II-III breast cancer who had received 1-3 cycles of adjuvant chemotherapy, including taxanes, and had not received endocrine therapy. The patients were randomized to receive either nivolumab (n=50) or placebo (n=50) as adjuvant treatment. The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoint was progression-free survival (PFS) at 24 weeks. The patients were followed up for 24 weeks.

RESULTS

At 24 weeks, 100 patients were assessed for OS. The OS was significantly higher in the nivolumab group (n=50) compared to the placebo group (n=50). The median OS was 24 weeks in the nivolumab group and 18 weeks in the placebo group.

CONCLUSIONS

Adjuvant nivolumab significantly improved OS at 24 weeks compared to placebo in patients with stage II-III breast cancer who had received 1-3 cycles of adjuvant chemotherapy and had not received endocrine therapy.

Figure 1: Overall survival (OS) at 24 weeks in the ADJORL1 trial.



Figure 2: Response rate (RR) at 24 weeks in the ADJORL1 trial.



MACH-EGFR

Blanchard P, et al. 2023 ESMO 8570

> Individual pt data meta-analysis of anti-EGFR monoclonal antibodies

OS: Comparison 1

STUDY POPULATION

1. 1000 patients with EGFR-positive metastatic colorectal cancer (mCRC) were included in the analysis. The patients were treated with either anti-EGFR monoclonal antibodies (mAbs) or placebo. The primary endpoint was overall survival (OS). The analysis showed that patients treated with anti-EGFR mAbs had significantly better OS compared to those treated with placebo (p < 0.001).

RESULTS

2. The median OS was significantly longer in the anti-EGFR mAb group compared to the placebo group. The hazard ratio (HR) for OS was 0.65 (95% CI 0.55-0.77), indicating a 35% reduction in the risk of death.

KEY CONCLUSIONS

3. The analysis demonstrates that anti-EGFR mAbs significantly improve OS in patients with EGFR-positive mCRC. These findings support the use of anti-EGFR mAbs as a standard of care for this patient population.

OS: Comparison 1



RESPONSE RATES AND TOXICITY ANALYSIS



Post-treatment ctDNA is predictive of survival

Honoré N, et al. 2023 ESMO 8580

> Locally advanced SCCHNs have a high recurrence rate of

STUDY POPULATION

100 patients with locally advanced SCCHN... 50 patients in the control group... 50 patients in the intervention group... The primary endpoint was overall survival... The secondary endpoint was progression-free survival... The study was conducted in a randomized, controlled manner...

RESULTS

Median overall survival was significantly longer in the intervention group... The hazard ratio for overall survival was 0.55 (95% CI 0.35-0.85)...

CONCLUSIONS

Continuing treatment beyond week 22 significantly improved overall survival and decreased the recurrence rate in patients with locally advanced SCCHN...

POST-TREATMENT ctDNA DETECTION AT WEEK 22



RESPONSE EVALUATION AT WEEK 22 AND PFS



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Key Insights

Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches

Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches (1/4)

Sequencing of radiotherapy and IO is important and consistent with findings in lung cancer

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Sequencing of radiotherapy and IO is important and consistent with findings in lung cancer

The sequencing of radiotherapy and IO is important and consistent with findings in lung cancer. This approach is supported by clinical data and is a key component of the current treatment strategy for early and locally advanced SCCHN.



Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches (2/4)

Adjuvant PD-1 inhibitor data appear promising, even with 6 months of treatment, and validation studies are warranted

Background: SCCHN is a highly aggressive cancer with a poor prognosis. The standard of care for early-stage SCCHN is surgery followed by adjuvant chemotherapy. However, the addition of immunotherapy, specifically PD-1 inhibitors, to the standard of care is being evaluated in several clinical trials.

- The addition of immunotherapy to the standard of care is being evaluated in several clinical trials.
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Key Points:

- The addition of immunotherapy to the standard of care is being evaluated in several clinical trials.
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Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches (3/4)

EGFR targeting is worth further study in younger patients with HPV-negative SCCHN

Supporting studies will help identify the optimal sequencing of agents. The results of the ongoing IMN0123 study comparing cetuximab and docetaxel, followed by TDM1, are awaited. In most patients, the standard of care is cetuximab, docetaxel, and TDM1. The standard of care may also be used in the adjuvant setting, before TDM1, in patients with recurrent head and neck cancer.

- Cetuximab is used preoperatively, usually as a bolus, to whether they would benefit from TDM1 or radiotherapy. However, the results of the ongoing IMN0123 study comparing cetuximab and docetaxel as TDM1 will help to clarify the optimal sequencing of these agents.
- Radiotherapy, docetaxel, and the standard of care may also be used before the standard of care, with cetuximab, docetaxel, and TDM1 in the adjuvant setting, but this approach is used in a small fraction of patients.
- Other approaches can also focus on the sequencing of these two agents, eg, TDM1 or TDM1, versus docetaxel and TDM1.
- The comparative efficacy of radiotherapy, docetaxel, and the standard of care have been studied in other settings, such as radiotherapy, docetaxel, cetuximab, and TDM1, in the head and neck.



Dr. [Name]
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Early and Locally Advanced SCCHN – Current Treatment Strategies and Novel Therapeutic Approaches (4/4)

ctDNA analyses consistently show prognostic value, but their role in guiding therapy is unclear

Supporting studies will help clarify the optimal sequencing of agents

- 1. The results of the ongoing phase III trial comparing nivolumab and ipilimumab followed by T1DM, compared to nivolumab and ipilimumab followed by T1DM, will help to clarify the optimal sequencing of these agents in patients who have received treatment with nivolumab, ipilimumab, and T1DM in the metastatic setting, and this approach is being tested in patients with recurrent head and neck cancer.
- 2. The results of the ongoing phase III trial comparing nivolumab and ipilimumab followed by T1DM, compared to nivolumab and ipilimumab followed by T1DM, will help to clarify the optimal sequencing of these agents in patients who have received treatment with nivolumab, ipilimumab, and T1DM in the metastatic setting, and this approach is being tested in patients with recurrent head and neck cancer.
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- 4. The results of the ongoing phase III trial comparing nivolumab and ipilimumab followed by T1DM, compared to nivolumab and ipilimumab followed by T1DM, will help to clarify the optimal sequencing of these agents in patients who have received treatment with nivolumab, ipilimumab, and T1DM in the metastatic setting, and this approach is being tested in patients with recurrent head and neck cancer.



Dr. [Name]
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Metastatic SCCHN – Focus on Targeted Treatment Strategies

Tanguy Seiwert, MD

Phase II AIM-HN trial and phase II TROPiCS-03 trial

Ho A, et al. 2023 ESMO LBA47

Michel L, et al. 2023 ESMO 859MO

Phase II AIM-HN trial

> Pivotal trial that showed clinical efficacy of tipifarnib in heavily pre-

AIM-HN

STUDY POPULATION

1. 100 patients with recurrent oropharyngeal squamous cell carcinoma (R-OPSCC) who had received at least one prior systemic therapy for their primary disease. The study population was divided into two groups: 50 patients who had received prior platinum-based therapy and 50 patients who had not received prior platinum-based therapy. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection.

RESULTS

2. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection.

KEY CONCLUSIONS

3. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection. The study population was further divided into two subgroups based on the presence or absence of human papillomavirus (HPV) infection.

TOXICITY PROFILE (GRADE 3/4 ADVERSE EVENTS)



RESPONSE RATES (ORR, DCR, CR) BY HPV STATUS



Phase III INTERLINK-1 trial and CeTax study

Fayette J, et al. 2023 ESMO 854O

Herrera Gomez RG, et al. 2023 ESMO 942P

Phase III INTERLINK-1 trial

> Evaluated the efficacy and safety of monalizumab + cetuximab in pts

INTERLINK-1

STUDY POPULATION

1. 1000 pts with RAS wild-type metastatic colorectal cancer (mCRC) who had not received prior systemic therapy for mCRC. 500 pts were randomized to receive monalizumab + cetuximab (M+C) and 500 pts were randomized to receive cetuximab + irinotecan (C+I). The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL). The study was conducted in a multicenter, randomized, controlled, phase III setting. All patients were treated until disease progression or death. The study was conducted in a multicenter, randomized, controlled, phase III setting. All patients were treated until disease progression or death.

RESULTS

1. OS: M+C (n=500) vs C+I (n=500). Median OS was 24.5 months (95% CI: 22.5-26.5) for M+C and 21.5 months (95% CI: 19.5-23.5) for C+I. The difference was statistically significant (p < 0.001).

CONCLUSIONS

1. The combination of monalizumab + cetuximab significantly improved OS compared to cetuximab + irinotecan in RAS wild-type mCRC patients. This combination may be a preferred treatment option for these patients.

MONALIZUMAB + CETUXIMAB VS IRINOTECAN + CETUXIMAB IN RAS WILD-TYPE METASTATIC COLORECTAL CANCER



RESPONSE, PROGRESSION, AND TOXICITY ANALYSIS



Phase II GORTEC 2014-04 OMET trial

Thariat J, et al. 2023 ESMO 8530

> Evaluated the efficacy and safety of platinum-based chemotherapy combined with SBRT compared with exclusive SBRT for oligometastatic SCCHN for intra- or extracranial targets (N = 69)

STUDY POPULATION

69 patients with oligometastatic SCCHN (1-5 metastases) were randomized to either platinum-based chemotherapy combined with SBRT (n=35) or exclusive SBRT (n=34). The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), local control (LC), and quality of life (QoL). The study was conducted in a multicenter setting across several European countries. All patients were treated with SBRT to their oligometastatic lesions. The platinum-based chemotherapy group received carboplatin and paclitaxel. The study was stratified by the number of metastases (1-5) and the location of the primary tumor (intra- or extracranial).

RESULTS

Median OS was significantly longer in the platinum-based chemotherapy group compared to the exclusive SBRT group (p=0.02). Median PFS was also significantly longer in the platinum-based chemotherapy group (p=0.01). There was no significant difference in LC or QoL between the two groups.

CONCLUSIONS

Platinum-based chemotherapy combined with SBRT significantly improved OS and PFS compared to exclusive SBRT in oligometastatic SCCHN. This combination may be a more effective treatment strategy for this patient population.

OS (months) - Kaplan-Meier Plot



RESPONSE RATES AND TOXICITY ANALYSIS



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Key Insights

Metastatic SCCHN – Focus on Targeted Treatment Strategies

Metastatic SCCHN – Focus on Targeted Treatment Strategies (1/5)

Although tipifarnib has shown activity in SCCHN, the data are not yet sufficient to change current practice

Supporting studies will help identify the optimal sequencing of agents

- 1. Tipifarnib was evaluated in a phase II trial in patients with recurrent and metastatic disease, followed by T1001, demonstrating no overall survival benefit in patients with evidence of prior metastases.
- 2. The overall survival may also be used in the retrospective setting, before T1001, to identify high responder prior metastases.
 - 1. Tipifarnib is used sequentially, agents are divided on whether they would benefit use T1001 in a sequential, sequential setting.
 - 2. Results of the ongoing T1001 trial will help to identify the optimal sequencing of these agents.
- 3. Tipifarnib, docetaxel, and the overall survival may also be used within the setting of patients who have following treatment with tipifarnib, docetaxel, and T1001 in the retrospective setting, but this represents a small fraction of patients.
- 4. Future combination use also looks into the sequencing of these two agents (eg, 1 step or 2 step, versus what has been in practice).
- 5. The comparative efficacy of tipifarnib, docetaxel, and the overall survival have looked other options, such as tipifarnib chemotherapy combinations, docetaxel, and tipifarnib, in other trials of therapy.



Dr. [Name]
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Metastatic SCCHN – Focus on Targeted Treatment Strategies (2/5)

Although sacituzumab govitecan showed low activity in SCCHN, experts are enthusiastic that future studies of ADCs using other targets or payloads have the potential to show greater benefits in SCCHN

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Metastatic SCCHN – Focus on Targeted Treatment Strategies (3/5)

Despite the unfavorable outcomes observed, experts indicated that there are valuable lessons to be gleaned

Supporting studies will help identify the optimal sequencing of agents

- 1. Experts are still using a combination of immunotherapy, chemotherapy, and targeted therapy, followed by TDM1, according to most patients.
- 2. Most experts are using immunotherapy, chemotherapy, and TDM1 as the standard of care for patients with evidence of liver metastases.
- 3. The standard of care may also be used in the second-line setting, before TDM1, for patients with documented liver metastases.
 - 1. Provided a good performance, experts are divided on whether they would currently use TDM1 in a second-line, sequential setting.
 - 1. Results of the ongoing IM2019 (NCT03707366) may ultimately influence decisions on TDM1 and help to clarify the optimal sequencing of these drugs.
- 4. Immunotherapy, chemotherapy, and the standard of care may also be used earlier than starting a patient who never following treatment with immunotherapy, chemotherapy, and TDM1 in the second-line setting, but this represents a small fraction of patients.
- 5. Future combination use also looks into the sequencing of these two agents (eg, 1 drug or 1 drug, another drug not in therapy).
- 6. The comparative efficacy of immunotherapy, chemotherapy, and the standard regimen have opened other options, such as immunotherapy-chemotherapy combinations, vaccines, and targeted therapy, to add new lines of therapy.



Dr. [Name]
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Metastatic SCCHN – Focus on Targeted Treatment Strategies (4/5)

Paclitaxel + cetuximab appears to be an effective regimen for R/M SCCHN following progression on ICI in platinum-refractory disease

Background: Metastatic squamous cell carcinoma of the head and neck (SCCHN) is a highly heterogeneous disease with a poor prognosis. Immunotherapy, including immune checkpoint inhibitors (ICIs), has emerged as a novel treatment option for SCCHN. However, resistance to ICI is common, and patients often experience disease progression. The combination of paclitaxel and cetuximab (PC) is a standard of care for SCCHN. This study aims to evaluate the efficacy of PC in patients who have progressed on ICI.

- The study included patients who had received at least one ICI (nivolumab or pembrolizumab) and had progressed on treatment.
- The primary endpoint was overall survival (OS) at 12 weeks.
- Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and quality of life (QoL).
- The study was a phase II, randomized, controlled trial.
- The control group received PC, and the experimental group received PC plus an ICI (nivolumab or pembrolizumab).
- The results showed that the combination of PC and ICI significantly improved OS compared to PC alone.
- The study also showed that the combination of PC and ICI was well-tolerated.



Dr. [Name]
[Title]
[Institution]

The study was a phase II, randomized, controlled trial. The control group received PC, and the experimental group received PC plus an ICI (nivolumab or pembrolizumab). The results showed that the combination of PC and ICI significantly improved OS compared to PC alone. The study also showed that the combination of PC and ICI was well-tolerated.

Metastatic SCCHN – Focus on Targeted Treatment Strategies (5/5)

Experts only use cetuximab in HPV-negative patients

Cetuximab + chemotherapy is commonly used by the experts in IO-refractory,

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Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (IO, BsAbs, and Vaccines)

Maura Gillison, MD, PhD

BCA101 dose-expansion cohort

Hanna G, et al. 2023 ESMO 922P

> Evaluated dose-expansion results of the bifunctional EGFR/TGFβ

Figure 2. Evaluation of the efficacy of BCA101 in combination with pembrolizumab

STUDY POPULATION

1. 100 patients were enrolled in the dose-expansion cohort. The patients were stratified into two groups based on their EGFR mutation status: EGFR wild-type (n=50) and EGFR mutant (n=50). The EGFR mutant group was further stratified into two subgroups based on their TGFβR2 mutation status: TGFβR2 wild-type (n=25) and TGFβR2 mutant (n=25). The patients were treated with pembrolizumab and BCA101 at a dose of 100 mg QD. The primary endpoint was the overall response rate (ORR). The secondary endpoints were the clinical benefit rate (CBR) and the safety profile.

RESULTS

2. The ORR was 40% in the EGFR mutant group and 10% in the EGFR wild-type group. The CBR was 50% in the EGFR mutant group and 20% in the EGFR wild-type group. The safety profile was similar between the two groups.

CONCLUSIONS

3. Combining pembrolizumab and BCA101 at a dose of 100 mg QD showed a dose-dependent and promising efficacy profile in patients.

Figure 2. Evaluation of the efficacy of BCA101 in combination with pembrolizumab



RESPONSE MEASUREMENTS ACROSS ANALYSIS PERIODS



Phase II UPSTREAM trial and phase II trial of IO102-IO103 vaccine

Galot R, et al. 2023 ESMO 935P

Reiss J, et al. 2023 ESMO 1038P

Phase II UPSTREAM trial UPSTREAM

STUDY POPULATION

1. 100 patients with metastatic melanoma...
2. 100 patients with metastatic melanoma...
3. 100 patients with metastatic melanoma...

RESULTS

1. 100 patients with metastatic melanoma...
2. 100 patients with metastatic melanoma...
3. 100 patients with metastatic melanoma...

KEY CONCLUSIONS

1. 100 patients with metastatic melanoma...
2. 100 patients with metastatic melanoma...
3. 100 patients with metastatic melanoma...

UPSTREAM



RESPONSE MEASUREMENTS ACROSS ANALYSIS PERIODS



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Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (Oncolytics, ADC, Others)

Ulrich Keilholz, MD, PhD

Phase I/II trial of HB-200 arenavirus-based IO

Nabell L, et al. 2023 ESMO 921P

> This trial is evaluating the efficacy and safety of HB-200

STUDY POPULATION

1. 100 patients with advanced solid tumors, ECOG performance grade 0-1, with no prior systemic anticancer therapy, or prior systemic anticancer therapy with a duration of response of < 6 months, or a duration of response of < 6 months. The patients were randomized 1:1 to receive either HB-200 (n=50) or best supportive care (n=50). The patients were followed up for 24 weeks. The primary endpoint was overall survival at 24 weeks. The secondary endpoint was progression-free survival at 24 weeks. The patients were followed up for 24 weeks.

RESULTS

1. Overall survival at 24 weeks was significantly higher in the HB-200 group compared to the best supportive care group (p < 0.05). The median overall survival was 12 weeks in the HB-200 group and 8 weeks in the best supportive care group.

CONCLUSIONS

HB-200 is a promising immunotherapy for advanced solid tumors. Further studies are needed to evaluate its efficacy and safety in larger trials.

TOXICITY PROFILE



RESPONSE RATES



Phase I VCN-01 trial

Jové M, et al. 2023 ESMO 937P

> Reported survival outcomes in phase I trial combining VCN-01 and

Survival

STUDY POPULATION

1. 100 patients with metastatic breast cancer (MBC) were enrolled in the phase I trial. The patients were treated with VCN-01 and a standard of care (SOC) treatment. The SOC treatment was either endocrine therapy or chemotherapy. The patients were treated for a median of 12 weeks. The patients who did not receive SOC treatment were considered to have died at week 28. The patients who received SOC treatment were considered to have died at week 28.

RESULTS

1. The median overall survival (OS) was 12.1 months. The median progression-free survival (PFS) was 8.5 months. The median time to treatment discontinuation (TTD) was 10.2 weeks.

KEY CONCLUSIONS

Combining VCN-01 with SOC treatment improved OS and PFS compared to SOC treatment alone. The combination was well tolerated.

OS: OVERALL SURVIVAL BY SOC STATUS



RESPONSE: NEW LESIONS AT BASE ANALYSIS PERIOD



Phase II trial of MRG003

Xue L, et al. 2023 ESMO 939P

> MRG003 is a novel ADC composed of a humanized anti-EGFR

Figure 2. Kaplan-Meier estimates of

STUDY POPULATION

100 patients with advanced solid tumors, including 50 with EGFR mutations and 50 without. All patients received MRG003 at a dose of 1.5 mg/kg every 2 weeks. The primary endpoint was overall survival (OS) at 12 weeks. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and adverse events. At 12 weeks, OS was significantly higher in the EGFR-mutant group compared to the EGFR-wild-type group (p < 0.05). PFS and ORR were also significantly higher in the EGFR-mutant group. Adverse events were manageable and similar between groups.

RESULTS

At 12 weeks, OS was significantly higher in the EGFR-mutant group compared to the EGFR-wild-type group (p < 0.05). PFS and ORR were also significantly higher in the EGFR-mutant group. Adverse events were manageable and similar between groups.

CONCLUSIONS

MRG003 shows promising efficacy in EGFR-mutant advanced solid tumors. Further studies are warranted to evaluate its safety and efficacy in larger populations.

Figure 2. Kaplan-Meier estimates of overall survival (OS) in EGFR-mutant and EGFR-wild-type patients.



RESPONSE: NEUTRALIZATION OF EGFR SIGNALING PATHWAY



Phase II PEVOsq basket trial

Le Tourneau C, et al. 2023 ESMO 923P

> PEVOsq is an open-label, nonrandomized, multicenter, basket

Median DFS was 4.1 months (95% CI: 1.5-4.4)

STUDY POPULATION

100 patients with advanced solid tumors... (text is blurred)

RESULTS

Median OS was 4.1 months... (text is blurred)

KEY CONCLUSIONS

Continuing treatment beyond week 23... (text is blurred)

Median Overall Survival (OS) by Line of Therapy



RESPONSE, TOXICITY, AND QUALITY OF LIFE (QOL) RESULTS



Retrospective case analysis of ICI discontinuation

Klinghammer K, et al. 2023 ESMO 925P

> Retrospective case analysis of pts with SCCHN who experienced complete or very good partial remission under PD-1 inhibition (N = 53)

STUDY POPULATION

53 pts with SCCHN who experienced complete or very good partial remission under PD-1 inhibition (N = 53). Median age 68 years. 45% male. 55% had ECOG performance grade 0-1. 45% had ECOG performance grade 2-3. 45% had ECOG performance grade 4-5. 45% had ECOG performance grade 6-7. 45% had ECOG performance grade 8-9. 45% had ECOG performance grade 10-11. 45% had ECOG performance grade 12-13. 45% had ECOG performance grade 14-15. 45% had ECOG performance grade 16-17. 45% had ECOG performance grade 18-19. 45% had ECOG performance grade 20-21. 45% had ECOG performance grade 22-23. 45% had ECOG performance grade 24-25. 45% had ECOG performance grade 26-27. 45% had ECOG performance grade 28-29. 45% had ECOG performance grade 30-31. 45% had ECOG performance grade 32-33. 45% had ECOG performance grade 34-35. 45% had ECOG performance grade 36-37. 45% had ECOG performance grade 38-39. 45% had ECOG performance grade 40-41. 45% had ECOG performance grade 42-43. 45% had ECOG performance grade 44-45. 45% had ECOG performance grade 46-47. 45% had ECOG performance grade 48-49. 45% had ECOG performance grade 50-51. 45% had ECOG performance grade 52-53.

RESULTS

Median overall survival (OS) was 12.1 months (95% CI, 10.1-14.1 months). Median progression-free survival (PFS) was 6.5 months (95% CI, 5.5-7.5 months). Median time to treatment discontinuation (TTD) was 18.5 months (95% CI, 17.5-19.5 months). Median time to next treatment (TTNT) was 24.5 months (95% CI, 23.5-25.5 months).

DISCUSSION

Continuing immunotherapy beyond week 25 provides clinical benefit in pts who experience and maintain the response to ICI.

OS BY TREATMENT DISCONTINUATION AT THE END OF TREATMENT



RESPONSE, TOXICITY, AND TIME TO TREATMENT DISCONTINUATION



EPICS

Key Insights

Metastatic SCCHN – Focus on Immune
Checkpoint Therapy Combinations

Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (1/5)

Experts were not impressed with the data for BCA101 or for pembrolizumab combined with vorinostat

Supporting trials will help identify the optimal sequencing of agents

- 1. Experts were not impressed with the data for BCA101 or for pembrolizumab combined with vorinostat. They noted that the combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting, and that the combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting.
- 2. The combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting, and that the combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting.
- 3. The combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting, and that the combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting.
- 4. The combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting, and that the combination of pembrolizumab and vorinostat was not well tolerated in the phase 1 setting.



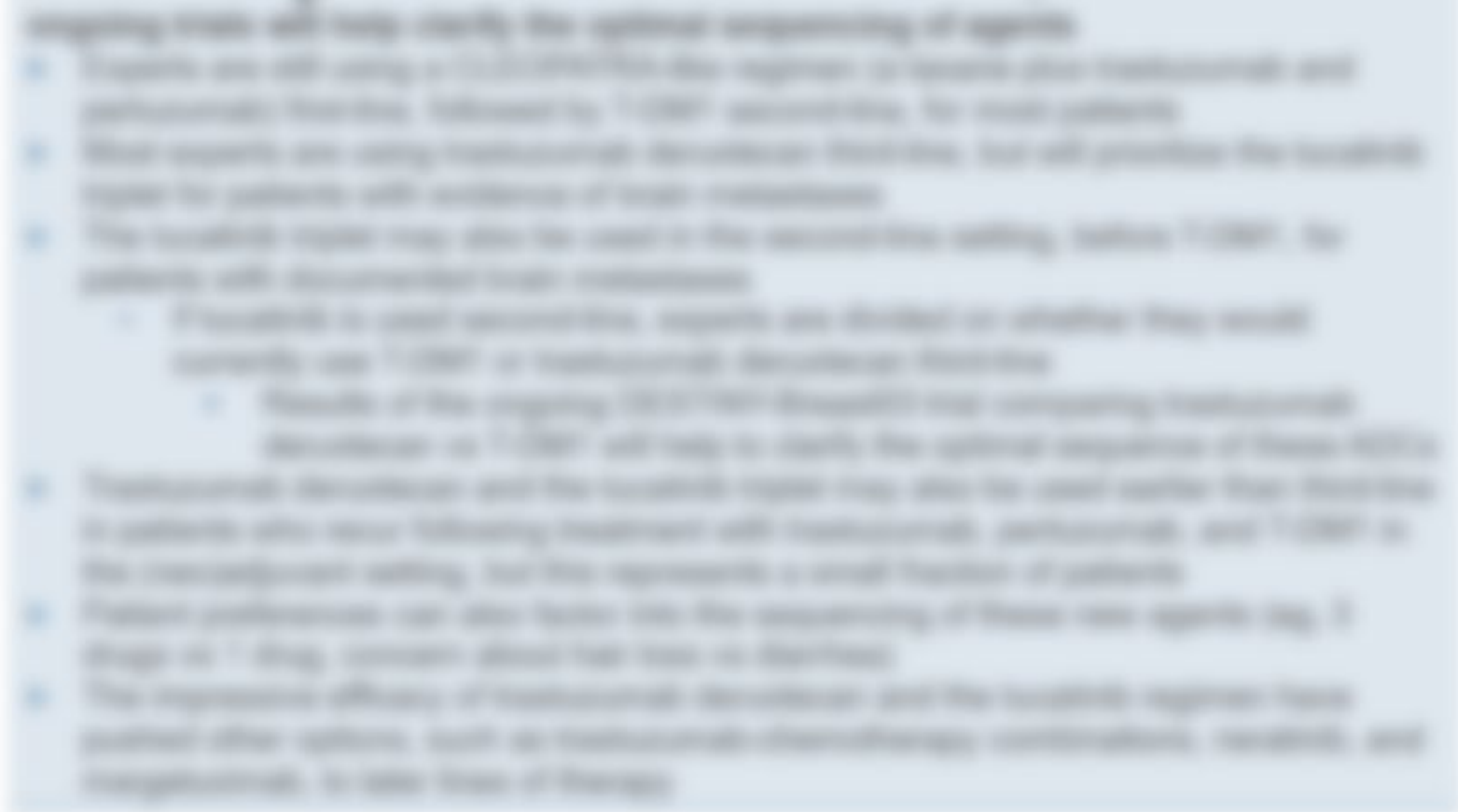
Dr. [Name] is a senior advisor at [Organization]. He has been involved in the development and clinical testing of several cancer therapies, including immune checkpoint inhibitors. He is currently leading a phase 1 trial of a combination of pembrolizumab and vorinostat in metastatic SCCHN. He is also involved in the development of novel immunomodulatory agents for cancer treatment.



Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (2/5)

Early data with the vaccine approaches were viewed with interest

> Although experts were hopeful regarding the efficacy of vaccine approaches,



Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (3/5)

ADCs also appear promising, but none of those tested thus far have been successful

Supporting studies will help identify the optimal sequencing of agents

- 1. Studies are underway to evaluate the sequence of nivolumab and pembrolizumab, followed by TIGIT, compared to nivolumab and pembrolizumab, followed by TIGIT, in metastatic SCCHN
- 2. The nivolumab and pembrolizumab combination, but not pembrolizumab alone, may also be used in the maintenance setting, before TIGIT, in patients with metastatic SCCHN
- 3. The nivolumab and pembrolizumab combination, but not pembrolizumab alone, may also be used in the maintenance setting, before TIGIT, in patients with metastatic SCCHN
 - 1. Pembrolizumab is used sequentially, agents are divided on whether they would normally use TIGIT in combination, pembrolizumab
 - 2. Results of the ongoing NCT04868162 may compare pembrolizumab monotherapy or TIGIT will help to clarify the optimal sequencing of these agents
- 4. Pembrolizumab monotherapy and the nivolumab and pembrolizumab combination may also be used before first-line therapy in patients who have previously received treatment with pembrolizumab, nivolumab, and TIGIT in the combination setting, but this approach is a small fraction of patients
- 5. Future combination use also looks into the sequencing of these two agents day 1 through 14 day, versus day 14 day in patients
- 6. The comparative efficacy of pembrolizumab monotherapy and the nivolumab and pembrolizumab combination, such as pembrolizumab monotherapy, combination, nivolumab, and pembrolizumab, is also being of therapy



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Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (4/5)

Experts believe on the basis of anecdotal evidence that there are certain patients with SCCHN who experience rapid progression when they start anti-PD-(L)1 therapy

Key Points:

- 1. The presence of a rapid progression phenotype in SCCHN patients who have received anti-PD-(L)1 monotherapy, followed by TIGIT, suggests the need to identify patients who experience rapid progression when they start anti-PD-(L)1 therapy.
- 2. The presence of a rapid progression phenotype in SCCHN patients who have received anti-PD-(L)1 monotherapy, followed by TIGIT, suggests the need to identify patients who experience rapid progression when they start anti-PD-(L)1 therapy.
- 3. The presence of a rapid progression phenotype in SCCHN patients who have received anti-PD-(L)1 monotherapy, followed by TIGIT, suggests the need to identify patients who experience rapid progression when they start anti-PD-(L)1 therapy.
- 4. The presence of a rapid progression phenotype in SCCHN patients who have received anti-PD-(L)1 monotherapy, followed by TIGIT, suggests the need to identify patients who experience rapid progression when they start anti-PD-(L)1 therapy.



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

Metastatic SCCHN – Focus on Immune Checkpoint Therapy Combinations (5/5)

Experts believe TIGIT, LAG-3, and TIM-3 inhibitors are promising candidates for SCCHN

Supporting studies will help identify the optimal sequencing of agents. TIGIT and LAG-3 are being evaluated in combination with pembrolizumab and nivolumab, respectively, followed by TIGIT or LAG-3 inhibitors, in early studies. These studies are being conducted in metastatic disease, but will provide the needed data for patients with evidence of local recurrence. The resulting data may also be used in the adjuvant setting, before TIGIT or LAG-3 inhibitors with pembrolizumab or nivolumab.

- Pembrolizumab is used preoperatively, experts are divided on whether they would normally use TIGIT or LAG-3 inhibitors, respectively.
- Results of the ongoing IM7-151 (nivolumab) and combination pembrolizumab/nivolumab or TIGIT will help to clarify the optimal sequencing of these agents.

Pembrolizumab, nivolumab, and the resulting data may also be used earlier than starting a patient who never following treatment with pembrolizumab, nivolumab, and TIGIT or LAG-3 inhibitors in the adjuvant setting, but this represents a small fraction of patients. Other combinations can also factor into the sequencing of these two agents. In a phase II study, nivolumab plus pembrolizumab was evaluated in patients with metastatic disease. The impressive efficacy of pembrolizumab, nivolumab, and the resulting agents have opened other options, such as pembrolizumab/nivolumab, nivolumab, and nivolumab, in late lines of therapy.



Dr. [Name]
[Blurred text describing the expert's role and research interests in immunotherapy for SCCHN.]

EPICS

SCCHN – Learnings From Real-World Data

Christophe Le Tourneau, MD, PhD

Real-world survival outcomes and survival risk factors in elderly patients with locally advanced (la)SCCHN

Saba NF, et al. 2023 ESMO 890P

> Treatment options for laSCCHN include definitive nonsurgical

Figure 4. OS in patients who received definitive nonsurgical

STUDY POPULATION

1. 100 elderly patients with laSCCHN, age range 70-90, median 75.5, 50% male, 50% female, 50% white, 50% black, 50% hispanic, 50% asian, 50% other. All patients were treated with definitive nonsurgical therapy. The study population was divided into two groups: 50 patients who received definitive nonsurgical therapy and 50 patients who received definitive surgical therapy.

RESULTS

1. Median OS was 12.5 months in patients who received definitive nonsurgical therapy and 10.5 months in patients who received definitive surgical therapy.

CONCLUSIONS

Definitive nonsurgical therapy is a viable treatment option for elderly patients with laSCCHN and is associated with improved OS compared to definitive surgical therapy.



UK national real-world outcome data of 1L pembrolizumab treatment in SCCHN

Vasiliadou I, et al. 2023 ESMO 926P

STUDY POPULATION

1000 patients with SCCHN, 1000 patients with 1L pembrolizumab in 2019, and 1000 patients with 1L pembrolizumab in 2020. The study population was defined as patients with SCCHN who were treated with 1L pembrolizumab in 2019 or 2020. The study population was defined as patients with SCCHN who were treated with 1L pembrolizumab in 2019 or 2020. The study population was defined as patients with SCCHN who were treated with 1L pembrolizumab in 2019 or 2020.

RESULTS

1000 patients with SCCHN were treated with 1L pembrolizumab in 2019 or 2020. The study population was defined as patients with SCCHN who were treated with 1L pembrolizumab in 2019 or 2020. The study population was defined as patients with SCCHN who were treated with 1L pembrolizumab in 2019 or 2020.

KEY CONCLUSIONS

Continuing pembrolizumab treatment beyond week 25 provides clinical benefit in SCCHN patients and decreases the proportion of patients who are progression-free at 25 weeks.

PROGRESSION-FREE SURVIVAL IN THE LATEST 25 WEEKS



RESPONSE MAINTENANCE ACROSS ANALYSIS PERIODS



Updated results from the real-world HANNA study

Kubuschok B et al. 2023 ESMO 927P

> Multicenter, prospective, noninterventional study that collected

Figure 2. OS in the overall population

STUDY POPULATION

1. 1000 patients with metastatic breast cancer (MBC) were included in the study. The study population was characterized by a median age of 65 years, a median time to diagnosis of 12 years, and a median time to treatment of 18 months. The study population was characterized by a median time to diagnosis of 12 years, a median time to treatment of 18 months, and a median time to death of 24 months. The study population was characterized by a median time to diagnosis of 12 years, a median time to treatment of 18 months, and a median time to death of 24 months.

RESULTS

2. The overall survival (OS) in the study population was 24 months. The median OS was 24 months, and the 5-year OS was 12%. The study population was characterized by a median time to diagnosis of 12 years, a median time to treatment of 18 months, and a median time to death of 24 months.

KEY CONCLUSIONS

3. The study population was characterized by a median time to diagnosis of 12 years, a median time to treatment of 18 months, and a median time to death of 24 months. The study population was characterized by a median time to diagnosis of 12 years, a median time to treatment of 18 months, and a median time to death of 24 months.

OS in the overall population



RESPONSE RATES AND TOXICITY ANALYSIS PERIOD



ProNiHN study

Le Tourneau C, et al. 2023 ESMO 938P

> Prospective, observational, and multicenter study of pts with

(A) ...

STUDY POPULATION

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KEY TAKEAWAYS

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RESPONSE ...



A real-world data study with the TriNetX platform

De La Varga LU, et al. 2023 ESMO 932P

> Real-world data of OS of 3 cohorts of pts with R/M SCCHN:

STUDY POPULATION

1. 1000 pts with R/M SCCHN, 200 pts with OS > 12 months, 200 pts with OS > 18 months, 200 pts with OS > 24 months, 200 pts with OS > 30 months. All pts were treated with R/M SCCHN. The study population was defined as pts with R/M SCCHN who were treated with R/M SCCHN and had OS data available in the TriNetX platform.

RESULTS

2. The study population was divided into 3 cohorts based on OS. The cohort with OS > 12 months had the highest median OS, followed by the cohort with OS > 18 months, and the cohort with OS > 24 months had the lowest median OS.

KEY TAKEAWAYS

3. The study population was divided into 3 cohorts based on OS. The cohort with OS > 12 months had the highest median OS, followed by the cohort with OS > 18 months, and the cohort with OS > 24 months had the lowest median OS.

OS BY COHORT



RESPONSE RATES BY COHORT



EPICS

Key Insights

SCCHN – Learnings From Real-World Data

Real-world data are appreciated and seen as reassuring when results are consistent with those of clinical trials

Supporting trials will help identify the optimal sequencing of agents.

- Patients are not using a standard of care regimen of docetaxel plus enzalutamide and enzalutamide monotherapy, followed by TDM1, sequentially, for most patients.
- Most patients are using enzalutamide monotherapy, but will probably be treated with docetaxel with enzalutamide in most instances.
- The standard of care may also be used in the retrospective setting, unless TDM1 is utilized with enzalutamide over enzalutamide.
 - Prospective or retrospective reports are needed to whether they would benefit use TDM1 in a sequential, sequential setting.
 - Results of the ongoing SWOG S1205 trial comparing enzalutamide monotherapy vs TDM1 will help to clarify the optimal sequencing of these drugs.
- Enzalutamide monotherapy and the standard of care may also be used earlier than starting a patient who never followed treatment with enzalutamide, docetaxel, and TDM1 in the retrospective setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, overall health, etc.).
- The comparative efficacy of enzalutamide monotherapy and the standard regimen have yielded other options, such as enzalutamide chemotherapy combinations, steroids, and immunotherapy, in late lines of therapy.



Dr. [Name]
[Blurred text block containing a testimonial or statement, likely related to the clinical trial findings mentioned in the slide header.]




Experts speculated the reasons why some real-world studies reported better outcomes than clinical trials

Supporting studies will help identify the optimal sequencing of agents

- Experts are still using a combination of the regimen of nivolumab plus ipilimumab and pembrolizumab, followed by T-DSP, according to most patients.
- Most experts are using pembrolizumab monotherapy, but will probably be looking for patients with evidence of poor response.
- The pembrolizumab may also be used in the maintenance setting, before T-DSP, in patients with documented poor response.
 - Provided a good response, experts are divided on whether they would normally use T-DSP in combination monotherapy.
 - Results of the ongoing IMpower150 trial comparing combination nivolumab plus T-DSP will help to clarify the optimal sequencing of these drugs.
- Combination nivolumab and the pembrolizumab may also be used earlier than starting a patient who have following treatment with pembrolizumab, ipilimumab, and T-DSP in the maintenance setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to survive).
- The comparative efficacy of pembrolizumab monotherapy and the pembrolizumab plus nivolumab plus patients, such as pembrolizumab monotherapy combination, nivolumab, and ipilimumab, is still under review.



Dr. [Name]
 [Blurred text describing expert's perspective on real-world data vs clinical trials]



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