



EPICS

# EPICS: Global Perspectives in Melanoma

November 19, 2022

FULL REPORT

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Full Report	6 

EPICS

## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
November 19, 2022



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



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations

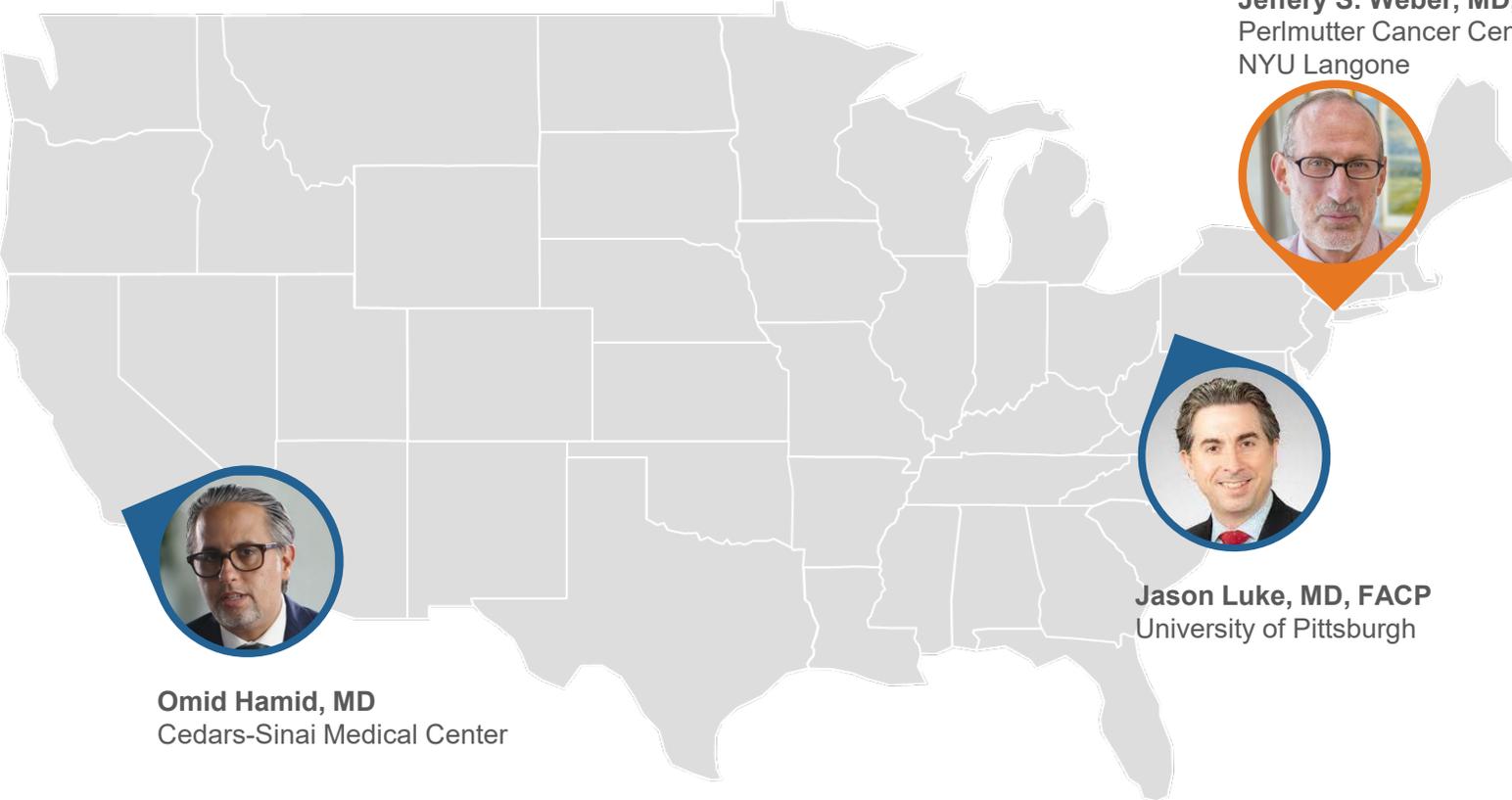


**PANEL:** Key experts in  
melanoma  
> 3 from US  
> 4 from Europe



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

# Panel Consisting of 3 US and 4 EU Melanoma Experts



**Omid Hamid, MD**  
Cedars-Sinai Medical Center

**Jason Luke, MD, FACP**  
University of Pittsburgh

**Chair**  
**Jeffery S. Weber, MD, PhD**  
Perlmutter Cancer Center at  
NYU Langone



**Alexander Eggermont, MD, PhD**  
Princess Máxima Center for  
Pediatric Oncology

**Axel Hauschild, MD, PhD**  
University Hospital  
Schleswig-Holstein

**Caroline Robert, MD, PhD**  
Gustave Roussy

**Reinhard Dummer, MD**  
University Hospital of Zurich

# Meeting Agenda: November 19

Time (EDT)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM (5 min)	Welcome and Introductions	Jeffrey S. Weber, MD, PhD
8.05 AM – 8.15 AM (10 min)	Prognostic and Predictive Markers in Melanoma	Jason Luke, MD, FACP
8.15 AM – 8.35 AM (20 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
8.35 AM – 8.45 AM (10 min)	Adjuvant and Neoadjuvant Therapies in Melanoma: What Is New There?	Alexander Eggermont, MD, PhD
8.45 AM – 9.10 AM (25 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
9.10 AM – 9.20 AM (10 min)	Evolution of Immunotherapy for First-Line Metastatic Melanoma	Jeffrey S. Weber, MD, PhD
9.20 AM – 9.45 AM (25 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
9.45 AM – 9.55 AM (10 min)	Emerging Insights in Relapsed/Refractory Metastatic Melanoma	Omid Hamid, MD
9.55 AM – 10.20 AM (25 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
10.20 AM – 10.30 AM (10 min)	BREAK	
10.30 AM – 10.40 AM (10 min)	<i>BRAF</i> -Mutated Melanoma: New Developments or Stagnation?	Caroline Robert, MD, PhD
10.40 AM – 11.00 AM (20 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
11.00 AM – 11.10 AM (10 min)	New Perspectives in the Management of SCC	Axel Hauschild, MD, PhD
11.10 AM – 11.30 AM (20 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
11.30 AM – 11.40 AM (10 min)	Emerging Advances in the Management of BCC	Reinhard Dummer, MD
11.40 AM – 12.00 PM (20 min)	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
12.00 PM	Closing Remarks	Moderator: Jeffrey S. Weber, MD, PhD

EPICS

# Prognostic and Predictive Markers in Melanoma

Jason Luke, MD, FACP



# Prognostic and Predictive Markers in Melanoma (1/2)

Presented by Jason Luke, MD, FACP

## Advances in melanoma biomarkers

> Although advances have been made with melanoma

## Immunotherapy is SOC for all patients

> IPI + NIVO was approved for PD-L1–negative disease on the basis of





# Prognostic and Predictive Markers in Melanoma (2/2)

Presented by Jason Luke, MD, FACP

## Emerging biomarkers

> Neutrophil-lymphocyte ratio (NLR; abstract 871P) analysis from the

## Adjuvant setting

> The majority of patients are now eligible for adjuvant/ perioperative



# Discussion: Prognostic and Predictive Markers in Melanoma (1/2)

## Biomarker

The experts agreed that while developments have been made identifying prognostic and predictive biomarkers, more understanding is needed to utilize them in the clinic as reliable biomarkers

### STUDY POPULATION

1. 1000 patients with melanoma, 500 with BRAF V600E mutation and 500 without. All patients were treated with ipilimumab. The study was a phase III, randomized, controlled trial. The primary endpoint was overall survival. The secondary endpoint was progression-free survival. The study was conducted in a multicenter setting. The study was conducted in a multicenter setting. The study was conducted in a multicenter setting.

### RESULTS

1. The median overall survival was 12.1 months in the BRAF V600E mutation group and 10.1 months in the non-mutation group. The difference was statistically significant. The median overall survival was 12.1 months in the BRAF V600E mutation group and 10.1 months in the non-mutation group. The difference was statistically significant.

### CONCLUSIONS

1. The study demonstrated that ipilimumab treatment improved overall survival in patients with BRAF V600E mutation and decreased the mortality rate in patients with melanoma.

### PROGNOSTIC MARKERS IN MELANOMA



### PREDICTIVE MARKERS IN MELANOMA



# Discussion: Prognostic and Predictive Markers in Melanoma (2/2)

## Biomarker

**PD-L1 staining in newly diagnosed patients is not routinely ordered by the experts, especially those in Europe**

> The discussion on the necessity of PD-L1 staining has resurfaced in Europe due to RELA + NIVO EMA approval; however, 1 expert noted

**STUDY POPULATION**

1. 1000 newly diagnosed melanoma patients with a 100% PD-L1 staining rate in 2015. The study population was divided into two groups: 500 patients with a 100% PD-L1 staining rate and 500 patients with a 0% PD-L1 staining rate. The study population was followed up for 12 months. The results showed that the 100% PD-L1 staining group had a significantly higher survival rate compared to the 0% PD-L1 staining group.

**RESULTS**

1. The 100% PD-L1 staining group had a significantly higher survival rate compared to the 0% PD-L1 staining group. The results showed that the 100% PD-L1 staining group had a significantly higher survival rate compared to the 0% PD-L1 staining group.

**KEY TAKEAWAYS**

1. PD-L1 staining is a prognostic marker in melanoma. The results showed that the 100% PD-L1 staining group had a significantly higher survival rate compared to the 0% PD-L1 staining group.

**PD-L1 STAINING IN NEWLY DIAGNOSED PATIENTS**

Region	PD-L1 Staining Rate (%)
North America	15
Europe	10
Asia	20
Australia	18
South America	12
Africa	14
Oceania	16

**PD-L1 STAINING IN NEWLY DIAGNOSED PATIENTS**

Region	Time Point	PD-L1 Staining Rate (%)
North America	2015	15
	2016	18
Europe	2015	10
	2016	12
Asia	2015	20
	2016	22
Australia	2015	18
	2016	20
South America	2015	12
	2016	14
Africa	2015	14
	2016	16
Oceania	2015	16
	2016	18

EPICS

# Adjuvant and Neoadjuvant Therapies in Melanoma: What Is New There?

Alexander Eggermont, MD, PhD



# Adjuvant and Neoadjuvant Therapies in Melanoma: What Is New There? (1/2)

Presented by Alexander Eggermont, MD, PhD

## Adjuvant trial updates

> The 5-year follow-up for KEYNOTE-054 exploring adjuvant

## CheckMate 76K

> CheckMate 76K reported that NIVO treatment in patients with completely

**STUDY POPULATION**

KEYNOTE-054 was a phase III, randomized, controlled trial comparing adjuvant pembrolizumab (1 mg/kg intravenous [IV] every 3 weeks for 1 year) with placebo in patients with completely resected melanoma. The primary endpoint was overall survival (OS). The secondary endpoints were disease-free survival (DFS), relapse-free survival (RFS), and time to distant recurrence (TDR). The trial was stratified by Breslow thickness (≤1 mm vs >1 mm) and ulceration (yes vs no).

**RESULTS**

At 5 years, OS was significantly higher in the pembrolizumab group compared with the placebo group (54.1% vs 48.1%, p=0.0001). DFS, RFS, and TDR were also significantly higher in the pembrolizumab group.

**CONCLUSIONS**

Adjuvant pembrolizumab significantly improved OS, DFS, RFS, and TDR in patients with completely resected melanoma.

**CheckMate 76K**

**RESPONSE, RECURRENT, AND DISEASE-FREE SURVIVAL**



# Adjuvant and Neoadjuvant Therapies in Melanoma: What Is New There? (2/2)

Presented by Alexander Eggermont, MD, PhD

## Neoadjuvant immunotherapy

> The benefits of neoadjuvant therapy include shorter treatment time.

## Deferring surgery where possible

> The PRADO trial found that surgery can be deferred in



# Discussion: Adjuvant and Neoadjuvant Therapies in Melanoma – What Is New There? (1/2)

## Adjuvant

Adjuvant therapy should be considered for all patients, especially those who may not benefit from neoadjuvant treatment

**STAGE POPULATION**

1. 1000 patients with stage I-III melanoma, randomized to 1000 mg of pembrolizumab or 100 mg of ipilimumab. 50% of patients received pembrolizumab, 50% received ipilimumab. The primary endpoint was overall survival. The secondary endpoint was progression-free survival. The tertiary endpoint was quality of life. The pembrolizumab group had significantly better overall survival, progression-free survival, and quality of life compared to the ipilimumab group.

**RESULTS**

1. Overall survival: 1000 patients, pembrolizumab 50%, ipilimumab 50%. Median overall survival: pembrolizumab 26.3 months, ipilimumab 22.2 months. Hazard ratio: 0.82 (95% CI 0.68-0.99).

**KEY TAKEAWAYS**

1. Pembrolizumab significantly improved overall survival, progression-free survival, and quality of life compared to ipilimumab in stage I-III melanoma.



# Discussion: Adjuvant and Neoadjuvant Therapies in Melanoma – What Is New There? (2/2)

## Neoadjuvant therapy

The experts agreed that neoadjuvant treatment has great potential in locally advanced disease



**STUDY POPULATION**

1. 1000 patients with melanoma, 500 in each arm. The neoadjuvant arm received nivolumab and ipilimumab for 12 weeks, followed by resection. The control arm received resection followed by nivolumab and ipilimumab for 12 weeks. The primary endpoint was overall survival at 5 years. Secondary endpoints included time to recurrence, distant recurrence-free survival, and quality of life.

**RESULTS**

1. The 5-year overall survival was significantly higher in the neoadjuvant arm (55%) compared to the control arm (45%). Time to recurrence and distant recurrence-free survival were also significantly improved in the neoadjuvant arm. Quality of life was similar between the two arms.

**KEY CONCLUSIONS**

1. Neoadjuvant treatment with nivolumab and ipilimumab significantly improved overall survival and time to recurrence in patients with melanoma.

**KEY POINTS FROM THE STUDY**

Arm	5-year Overall Survival (%)
Neoadjuvant (Nivolumab + Ipilimumab)	55%
Control (Resection + Nivolumab + Ipilimumab)	45%

**RESPONSE RATES AND TOXICITY**

Parameter	Neoadjuvant Arm (%)	Control Arm (%)
Objective Response Rate	~75%	~45%
Grade 3/4 Toxicity	~15%	~10%

EPICS

# Evolution of Immunotherapy for First-Line Metastatic Melanoma

Jeffrey S. Weber, MD, PhD



# Evolution of Immunotherapy for First-Line Metastatic Melanoma

Presented by Jeffrey S. Weber, MD, PhD

## Important updates

> The RELATIVITY-047 trial reported improved PFS, OS, and

*[Blurred content area]*

## Tumor-infiltrating lymphocytes

> TIL treatment remains a second-line option for PD-1–refractory

*[Blurred diagram showing two circular representations of tumor cells with lymphocytes infiltrating them. The left circle shows more lymphocyte infiltration than the right circle.]*



# Discussion: Evolution of Immunotherapy for First-Line Metastatic Melanoma (1/2)

## Current practices and beyond

Although the use of combination regimens is becoming more frequent in the front line, there is still



*[Blurred text block]*

*[Blurred text block]*

*[Blurred text block]*

# Discussion: Evolution of Immunotherapy for First-Line Metastatic Melanoma (2/2)

## KEY TAKEAWAYS

The evolution of immunotherapy for first-line metastatic melanoma has been driven by the development of immune checkpoint inhibitors. These drugs, including ipilimumab, nivolumab, and pembrolizumab, have significantly improved survival outcomes for patients with advanced melanoma. The combination of ipilimumab and nivolumab is now the standard of care for first-line treatment of metastatic melanoma. The addition of pembrolizumab to the combination of ipilimumab and nivolumab has further improved outcomes, and this combination is also being evaluated in ongoing clinical trials.

## KEY POINTS

1. The combination of ipilimumab and nivolumab is the standard of care for first-line treatment of metastatic melanoma.

2. The addition of pembrolizumab to the combination of ipilimumab and nivolumab has further improved outcomes, and this combination is also being evaluated in ongoing clinical trials.

3. The evolution of immunotherapy for first-line metastatic melanoma has been driven by the development of immune checkpoint inhibitors.



Immunotherapy has revolutionized the treatment of melanoma, offering patients with advanced disease a new hope for long-term survival. The combination of immune checkpoint inhibitors, such as ipilimumab and nivolumab, has become the standard of care for first-line treatment of metastatic melanoma. The addition of pembrolizumab to this combination has further improved outcomes, and this combination is also being evaluated in ongoing clinical trials. The evolution of immunotherapy for first-line metastatic melanoma has been driven by the development of immune checkpoint inhibitors.



EPICS

# Emerging Insights in Relapsed/Refractory Metastatic Melanoma

Omid Hamid, MD



# Emerging Insights in Relapsed/Refractory Metastatic Melanoma (1/2)

Presented by Omid Hamid, MD



## ESMO updates

> Stopa et al reported no difference in PFS and treatment response with BRAF/MEK inhibitor and anti-PD-1 therapies in the first and second

**Background**

... ..

**Methods**

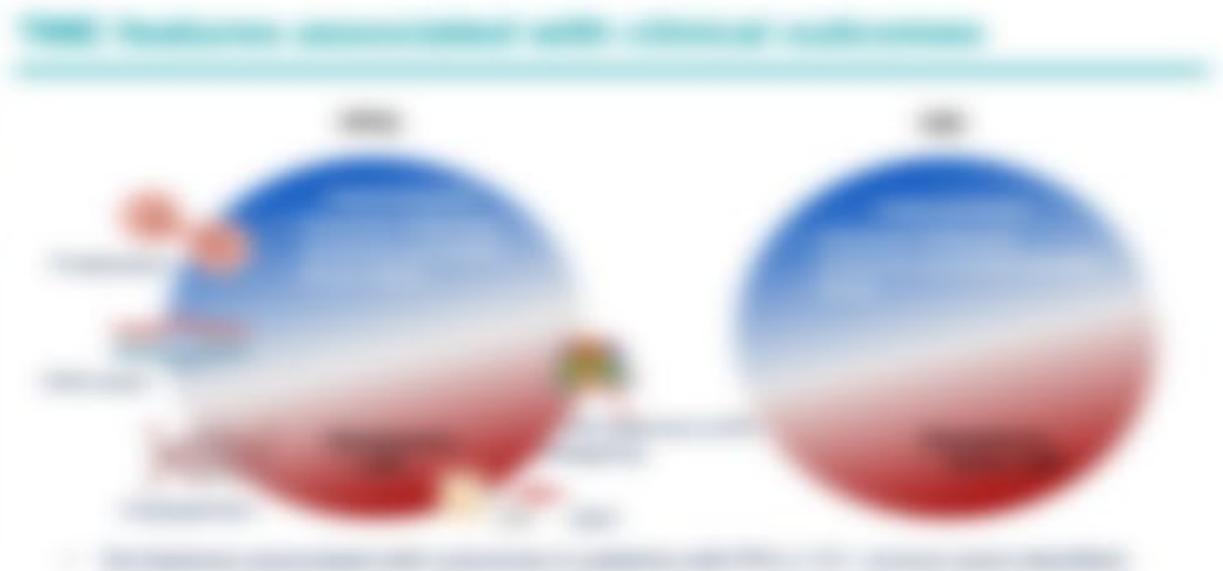
... ..

**Results**

... ..

**Conclusion**

... ..





# Emerging Insights in Relapsed/Refractory Metastatic Melanoma (2/2)

Presented by Omid Hamid, MD

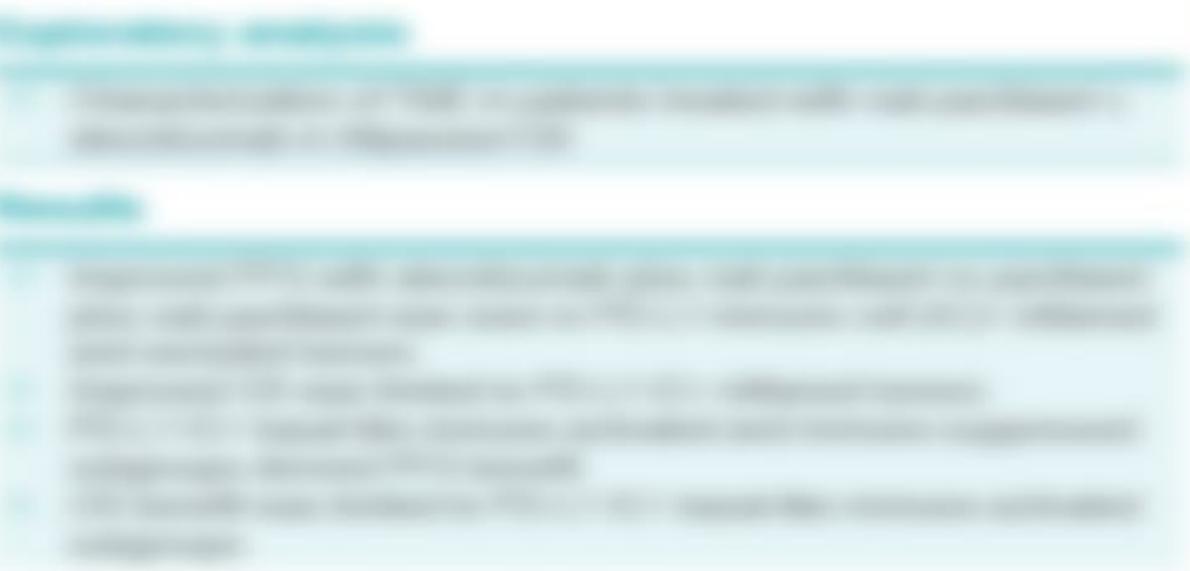


## Alternative TIL approaches

> Lifileucel (LN-144), an autologous TIL, demonstrated promising

## Preliminary but promising approaches

> Another interesting approach is with IOV-4001, a genetically



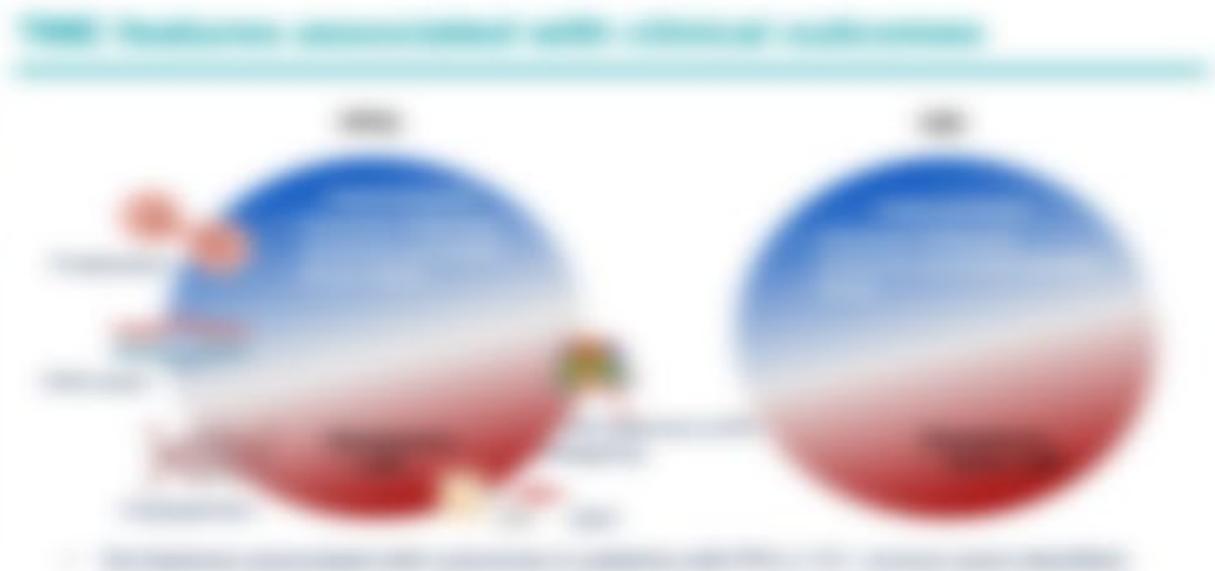
# Discussion: Emerging Insights in Relapsed/Refractory Metastatic Melanoma (1/2)

## Treatment landscape updates

The experts agreed there have been no recent practice-changing data, and there is a high medical need to improve second-line strategies

**Key Takeaways**

- There is a high medical need to improve second-line strategies in relapsed/refractory metastatic melanoma.
- Current treatment options include immunotherapy, targeted therapy, and combination approaches.
- Emerging insights suggest the need for novel agents and combination strategies to improve outcomes.



**Key Takeaways**

- There is a high medical need to improve second-line strategies in relapsed/refractory metastatic melanoma.
- Current treatment options include immunotherapy, targeted therapy, and combination approaches.
- Emerging insights suggest the need for novel agents and combination strategies to improve outcomes.

# Discussion: Emerging Insights in Relapsed/Refractory Metastatic Melanoma (2/2)

## Treatment landscape updates

Newer anti-CTLA-4 therapies have shown effective responses in other cancers, such as GI and ovarian, but it is yet to be determined

**Keynote-022**

Phase III trial comparing ipilimumab + nivolumab to ipilimumab + placebo in melanoma. The combination showed significantly higher overall survival compared to the control group.

**CheckMate-067**

Phase III trial comparing nivolumab + ipilimumab to nivolumab + placebo in melanoma. The combination showed significantly higher overall survival compared to the control group.

**CheckMate-067**

The diagrams illustrate the mechanism of action of the combination therapy. The left diagram shows a T cell (blue) interacting with a melanoma cell (red). A red arrow points to the CTLA-4 receptor on the T cell, indicating inhibition. The right diagram shows a T cell (blue) interacting with a melanoma cell (red). A red arrow points to the PD-1 receptor on the T cell, indicating inhibition.

**CheckMate-067**

Phase III trial comparing nivolumab + ipilimumab to nivolumab + placebo in melanoma. The combination showed significantly higher overall survival compared to the control group.



EPICS

# ***BRAF*-Mutated Melanoma: New Developments or Stagnation?**

Caroline Robert, MD, PhD



# BRAF-Mutated Melanoma: New Developments or Stagnation? (1/2)

Presented by Caroline Robert, MD, PhD

## Combination regimens

> There are limited options for BRAF-mutant patients after immunotherapy

## Triplet combination

> The spartalizumab + dabrafenib and trametinib (Sparta-





# BRAF-Mutated Melanoma: New Developments or Stagnation? (2/2)

Presented by Caroline Robert, MD, PhD

## High tumor burden

> The Sparta-DabTram regimen was investigated in patients with  $\geq 3$

## BRAF/MEK inhibitor resistance

> Vorinostat, a HDAC inhibitor with specificity for histone





# Discussion: *BRAF*-Mutated Melanoma – New Developments or Stagnation? (2/2)

## Treatment after progression

The experts agreed that a patient with a *BRAF* mutation could go directly to a trial and avoid



*[Blurred content area]*

*[Blurred content area]*

EPICS

# New Perspectives in the Management of SCC

Axel Hauschild, MD, PhD



# New Perspectives in the Management of SCC (1/2)

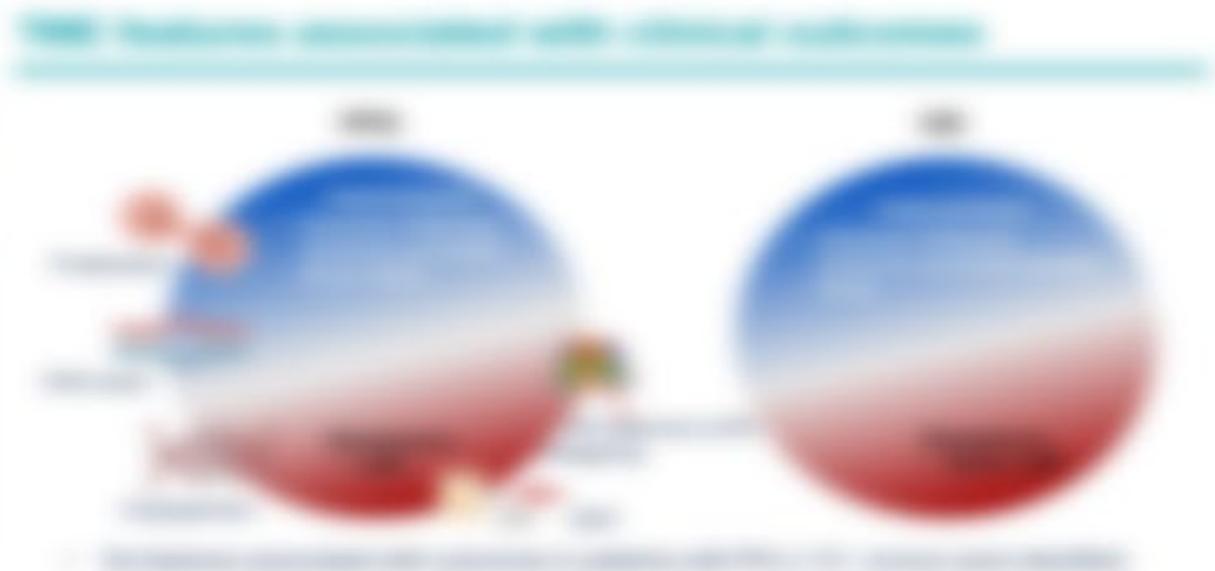
Presented by Axel Hauschild, MD, PhD

## Neoadjuvant cemiplimab

> Neoadjuvant cemiplimab treatment in locally advanced,

## Cemiplimab remains SOC

> The final analysis from EMPOWER-CSCC-1 reported an ORR of





# New Perspectives in the Management of SCC (2/2)

Presented by Axel Hauschild, MD, PhD

## Cemiplimab without surgery

> Cemiplimab demonstrated an ORR of 37.4% in patients with locally advanced or metastatic CSCC who are not candidates for curative

**Background**

... (blurred text) ...

**Objective**

... (blurred text) ...

**Methods**

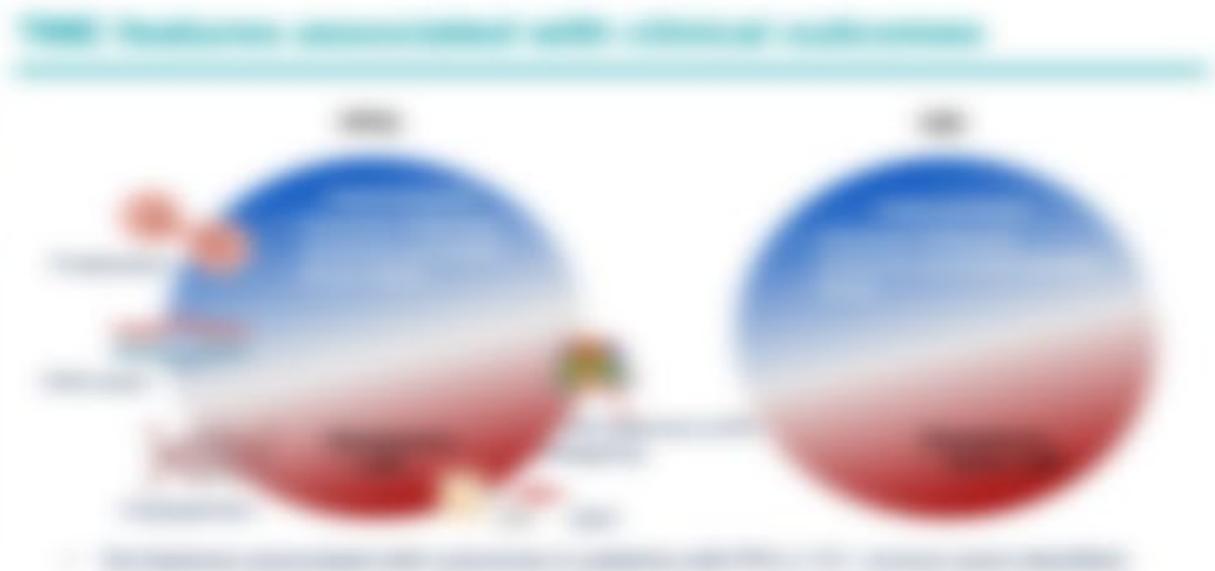
... (blurred text) ...

**Results**

... (blurred text) ...

**Conclusion**

... (blurred text) ...



**Discussion**

... (blurred text) ...

**Conclusion**

... (blurred text) ...



# Discussion: New Perspectives in the Management of SCC (1/2)

## Neoadjuvant therapy to reduce disfigurement

The experts agreed that the most exciting data came from the cemiplimab trials in both locally advanced and metastatic SCC

The experts stated that the results from the phase II trial (NCT01454042, ESMO abstract 780Q) are



**Background**

SCC is a common type of skin cancer. It can be treated with surgery, radiation, or a combination of both. Neoadjuvant therapy is given before surgery to reduce the size of the tumor and improve the chances of a complete response. This can lead to less disfigurement and better cosmetic outcomes.

**Objective**

To evaluate the efficacy and safety of neoadjuvant therapy in the management of SCC.

**Methods**

A phase II trial was conducted to evaluate the efficacy and safety of neoadjuvant therapy in the management of SCC. The trial compared the use of cemiplimab (an immune checkpoint inhibitor) with standard of care (SOC) in patients with locally advanced and metastatic SCC.

**Results**

The results of the trial showed that patients who received neoadjuvant therapy with cemiplimab had a significantly higher rate of complete response (CR) compared to those who received SOC. This was true for both locally advanced and metastatic SCC. Additionally, patients who received neoadjuvant therapy had significantly less disfigurement and better cosmetic outcomes compared to those who received SOC.

**Conclusion**

Neoadjuvant therapy with cemiplimab is an effective and safe treatment option for patients with locally advanced and metastatic SCC. It can lead to a higher rate of CR and improved cosmetic outcomes.

**Background**

SCC is a common type of skin cancer. It can be treated with surgery, radiation, or a combination of both. Neoadjuvant therapy is given before surgery to reduce the size of the tumor and improve the chances of a complete response. This can lead to less disfigurement and better cosmetic outcomes.

**Objective**

To evaluate the efficacy and safety of neoadjuvant therapy in the management of SCC.

**Methods**

A phase II trial was conducted to evaluate the efficacy and safety of neoadjuvant therapy in the management of SCC. The trial compared the use of cemiplimab (an immune checkpoint inhibitor) with standard of care (SOC) in patients with locally advanced and metastatic SCC.

**Results**

The results of the trial showed that patients who received neoadjuvant therapy with cemiplimab had a significantly higher rate of complete response (CR) compared to those who received SOC. This was true for both locally advanced and metastatic SCC. Additionally, patients who received neoadjuvant therapy had significantly less disfigurement and better cosmetic outcomes compared to those who received SOC.

**Conclusion**

Neoadjuvant therapy with cemiplimab is an effective and safe treatment option for patients with locally advanced and metastatic SCC. It can lead to a higher rate of CR and improved cosmetic outcomes.



# Discussion: New Perspectives in the Management of SCC (2/2)

## Novel therapies and resistance

There is potential for intralesional therapy in SCC, which also has a high mutational burden and is typically localized

**Background**

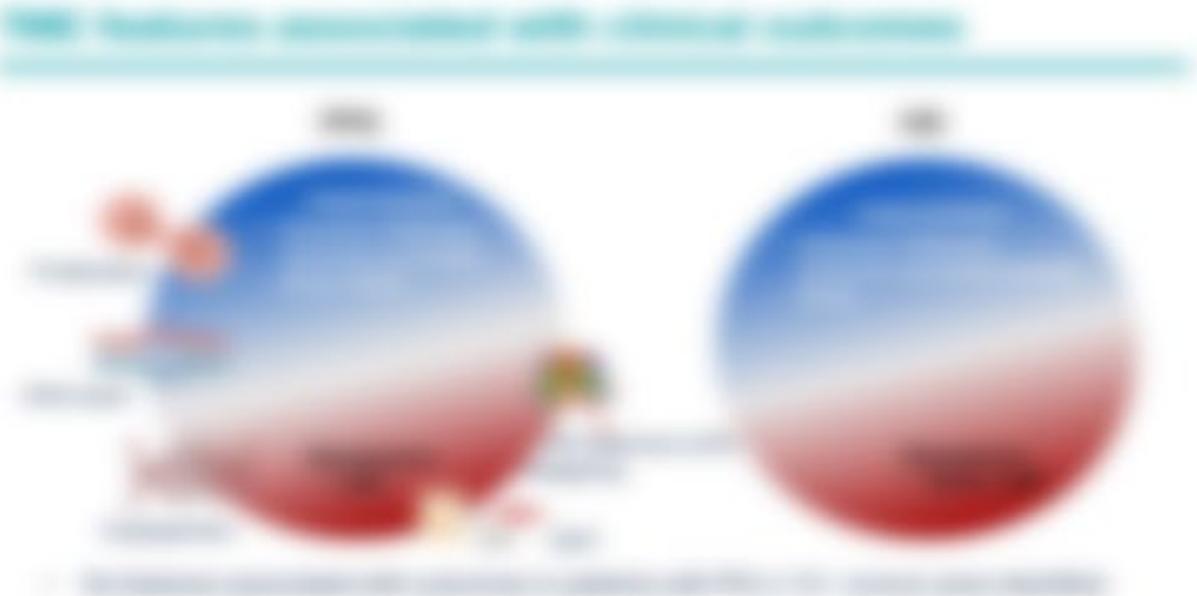
SCC is a common skin cancer with a high mutational burden. It is typically localized and has a high potential for resistance to systemic therapies. Intralesional therapy is a promising approach for localized SCC.

**Novel Therapies**

Novel therapies for SCC include immune checkpoint inhibitors, targeted therapies, and intralesional therapies. Intralesional therapies are designed to deliver high concentrations of drugs directly to the tumor site, potentially overcoming resistance to systemic therapies.

**Resistance**

Resistance to systemic therapies is a major challenge in the management of SCC. Intralesional therapy may be able to overcome resistance by delivering high concentrations of drugs directly to the tumor site.



EPICS

# Emerging Advances in the Management of BCC

Reinhard Dummer, MD



# Emerging Advances in the Management of BCC (1/2)

Presented by Reinhard Dummer, MD

## Hedgehog inhibitors

> As there is a large BCC patient population, there can often be complicated cases, such as those with genetic syndromes, rapid relapse,

*(This section contains blurred text, likely representing a list of references or detailed clinical notes.)*





# Emerging Advances in the Management of BCC (2/2)

Presented by Reinhard Dummer, MD

## Alternatives to HHI

> Neoadjuvant oncolytic viral therapy with talimogene laherparepvec (T-VEC) was well tolerated and showed high activity in difficult-to-resect



## Hedgehog inhibitors

Several experts would like to challenge the use of hedgehog inhibitors in the front line, as these agents have an associated chronic toxicity profile that is especially difficult to tolerate for elderly patients

*(This section contains blurred text, likely representing a list of references or detailed discussion points related to the topic of hedgehog inhibitors.)*

