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SCCHN in 2022 and Beyond

October 26, 2022

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Meeting Snapshot

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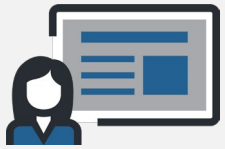
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
October 26, 2022



DISEASE-STATE AND DATA PRESENTATIONS
by key experts

INSIGHTS REPORT
including postmeeting analyses and actionable recommendations

PANEL: 6 key experts in SCCHN in 4 states in the US and 2 countries in Europe

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

Panel Consisting of 4 US and 2 European SCCHN Experts

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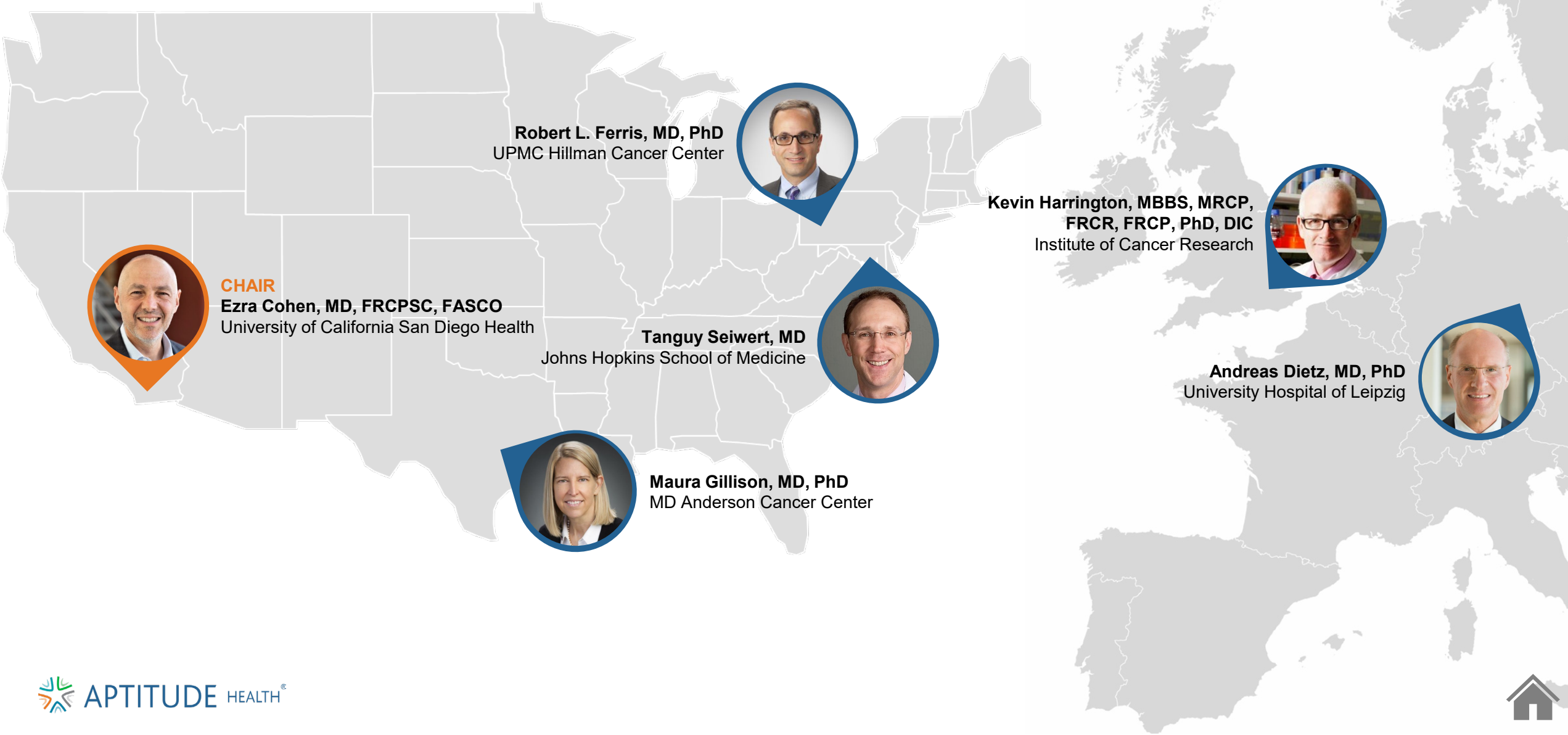

CHAIR
Ezra Cohen, MD, FRCPSC, FASCO
University of California San Diego Health

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

Kevin Harrington, MBBS, MRCP, FRCR, FRCP, PhD, DIC
Institute of Cancer Research

Andreas Dietz, MD, PhD
University Hospital of Leipzig

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Meeting Agenda

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Time	Topic	Speaker
11.00 AM – 11.05 AM	Welcome and Introductions	Ezra Cohen, MD, FRCPSC, FASCO
11.05 AM – 11.15 AM	Current Immune-Based Approaches • Neoadjuvant • First line	Robert Ferris, MD, PhD
11.15 AM – 11.35 AM	Discussion	
11.35 AM – 11.40 AM	Key Takeaways	
11.40 AM – 11.50 AM	Targeted Therapies, Alone or in Combination	Maura Gillison, MD, PhD
11.50 AM – 12.10 PM	Discussion	
12.10 PM – 12.15 PM	Key Takeaways	
12.15 PM – 12.25 PM	Immune Checkpoint Therapy Optimization	Tanguy Seiwert, MD
12.25 PM – 12.40 PM	Discussion	
12.40 PM – 12.45 PM	Key Takeaways	
12.45 PM – 12.55 PM	Immune Checkpoint Inhibitors: Relapsed/Metastatic	Kevin Harrington, MBBS, MRCP, FRCR, FRCP, PhD, DIC
12.55 PM – 1.20 PM	Discussion	
1.20 PM – 1.25 PM	Key Takeaways	
1.25 PM – 1.35 PM	Other Approaches (including investigational IOs)	Andreas Dietz, MD, PhD
1.35 PM – 1.50 PM	Discussion	
1.50 PM – 1.55 PM	Key Takeaways	
1.55 PM – 2.00 PM	Meeting Wrap-up	Ezra Cohen, MD, FRCPSC, FASCO

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Current Immune-Based Approaches

Robert Ferris, MD, PhD

UPMC Hillman Cancer Center

Abstracts Covered: Current Immune-Based Approaches

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- Neoadjuvant
  - 653O – Neoadjuvant nivolumab (N) before chemoradiation (CRT) in high-risk HPV driven

Primary results of the phase III KEYNOTE-412 study: Pembrolizumab (pembro) with chemoradiation therapy (CRT) vs placebo plus CRT for locally advanced (LA) head and neck squamous cell carcinoma (HNSCC)

Machiels et al. ESMO 2022. LBA5

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STUDY POPULATION (N = 804)

> Phase III trial in treatment-naive, unresected, LA HNSCC

PRIMARY ENDPOINT

Event-Free Survival, ITT Population

Data cutoff date: May 31, 2022

Phase II study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): Final analysis from EMPOWER-CSCC-1 groups 1, 2 and 3

Migden et al. ESMO 2022. 814P

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STUDY POPULATION (N = 193)

> Open-label, nonrandomized, multicenter, international phase II study in

ENDPOINTS

	Group 1	Group 2	Group 3

metastatic cutaneous squamous cell carcinoma; Q2W, every 2 weeks; Q3W, every 3 weeks.

Effects of durvalumab-metformin on head and neck squamous cell carcinoma (HNSCC)bas revealed by digital spatial profiling (DSP)

Riordan et al. ESMO 2022. 689P

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STUDY POPULATION (n = 8)

> Window of opportunity trial for durva + met in SCCHN

PRIMARY ENDPOINT

Nivolumab (Nivo) and ipilimumab (Ipi) combined with radiotherapy (RT) in patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN): Updated results on efficacy and correlative analysis

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Vathiotis et al. ESMO 2022. 672P

STUDY POPULATION (N = 24 [of whom 14 HPV positive])

> Patients with newly diagnosed stage IVA–B SCCHN of the oropharynx,

EFFICACY ENDPOINTS

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Current Immune-Based Approaches

Key Takeaways

Key Takeaways: Current Immune-Based Approaches

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- We continue to see data in SCCHN, but the standard of care has not changed

Discussion Highlight: Current Immune-Based Approaches

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RECENT UPDATES AND ADVANCES IN IMMUNOTHERAPY FOR SCCHN TREATMENT

Of the studies presented, KEYNOTE-412 most impressed the panel of experts, but it raised several questions

[illegible]

- [illegible]

[illegible]

- [illegible]

[illegible]

- [illegible]

[illegible]

- [illegible]

[illegible]

- [illegible]

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Targeted Therapies, Alone or in Combination

Maura Gillison, MD, PhD

MD Anderson Cancer Center

Abstracts Covered: Targeted Therapies, Alone or in Combination

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- LBA33 – 5-year overall survival (OS) in patients (pts) with locally advanced squamous cell carcinoma of

5-year overall survival (OS) in patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) treated with xevinapant + chemoradiotherapy (CRT) vs placebo + CRT in a randomized, phase II study (1/2)

Bourhis et al. ESMO 2022. LBA33

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STUDY POPULATION (N = 96)

PRIMARY ENDPOINT

5-year overall survival (OS) in patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) treated with xevinapant + chemoradiotherapy (CRT) vs placebo + CRT in a randomized, phase II study (2/2)

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Bourhis et al. ESMO 2022. LBA33

Postoperative chemoradiation in combination with cetuximab followed by 6-months cetuximab maintenance in squamous cell carcinoma of the head and neck with high risk of locoregional recurrence

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Tamaskovics et al. ESMO 2022. 671P

Neoadjuvant chemotarget therapy with cetuximab, docetaxel, and cisplatin in locally advanced resectable oral/oropharygeal SCC: A multicenter phase III trial (Eagle trial)

Zhong et al. ESMO 2022 669P

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Real-world evidence of first-line cetuximab (CX) plus paclitaxel (PX) in recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN)

Cirauqui Cirauqui et al. ESMO 2022. 678P

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Targeted Therapies, Alone or in Combination

Key Takeaways

Key Takeaways: Targeted Therapies, Alone or in Combination

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> Experts are excited by the results from the phase II clinical trial with xevinapant.

Discussion Highlight: Targeted Therapies, Alone or in Combination

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EXPERTS WERE MOST IMPRESSED BY THE PHASE II RESULTS WITH

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Immune Checkpoint Therapy Optimization

Tanguy Seiwert, MD

Johns Hopkins School of Medicine

Abstracts Covered: Immune Checkpoint Therapy Optimization

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> 676P – ATHENA: A multicenter phase II of atezolizumab (A) and bevacizumab (B)

ATHENA: A multicenter phase II of atezolizumab and bevacizumab in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck – The HPV-negative cohort

Fayette et al. ESMO 2022 676P

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Evaluation of the DNA damage response network as predictor of nivolumab efficacy in head and neck squamous cell carcinoma

Economopoulou et al. ESMO 2022 661MO

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STUDY POPULATION (N = 76)

DATA

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OPTIM: A randomized phase II study on the OPTimization of IMmunotherapy in SCC of the head and neck – AIO-KHT-0117

Gruenwald et al. ESMO 2022 681P

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STUDY POPULATION (N = 154)

PRIMARY ENDPOINT

Next-generation sequencing (NGS) helps predict response to immunotherapy in recurrent or metastatic head and neck SCC patients

Mirallas et al. ESMO 2022 686P

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STUDY POPULATION (N = 96)

STUDY DATA

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Immune Checkpoint Therapy Optimization

Key Takeaways

Key Takeaways: Immune Checkpoint Therapy Optimization

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> The combination of anti–PD(L)-1 and anti-VEGF continues to be explored

Discussion Highlight: Immune Checkpoint Therapy Optimization (1/2)

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THE NEED FOR BIOMARKERS IS CLEAR. EXPERTS EAGERLY AWAIT A WAY TO MAXIMIZE TREATMENT EFFICACY USING A BIOMARKER-GUIDED APPROACH

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Discussion Highlight: Immune Checkpoint Therapy Optimization (2/2)

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THE BEST SEQUENCING OF IMMUNOTHERAPY FOR THE TREATMENT OF SCCHN IS STILL BEING INVESTIGATED

Single-agent nivolumab randomized to ipilimumab-nivolumab vs docetaxel is an evidence-free

“

Dr Harrington:

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Immune Checkpoint Inhibitors: Relapsed/Metastatic

Kevin Harrington, MBBS, MRCP, FRCR, FRCP, PhD, DIC

Institute of Cancer Research

Abstracts Covered: Immune Checkpoint Inhibitors in R/M SCCHN

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- 658MO – Pembrolizumab (pembro) vs standard-of-care (SOC) in previously treated recurrent/metastatic

Pembrolizumab (pembro) vs standard-of-care (SOC) in previously treated recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 6-year follow-up of KEYNOTE-040 (1/4)

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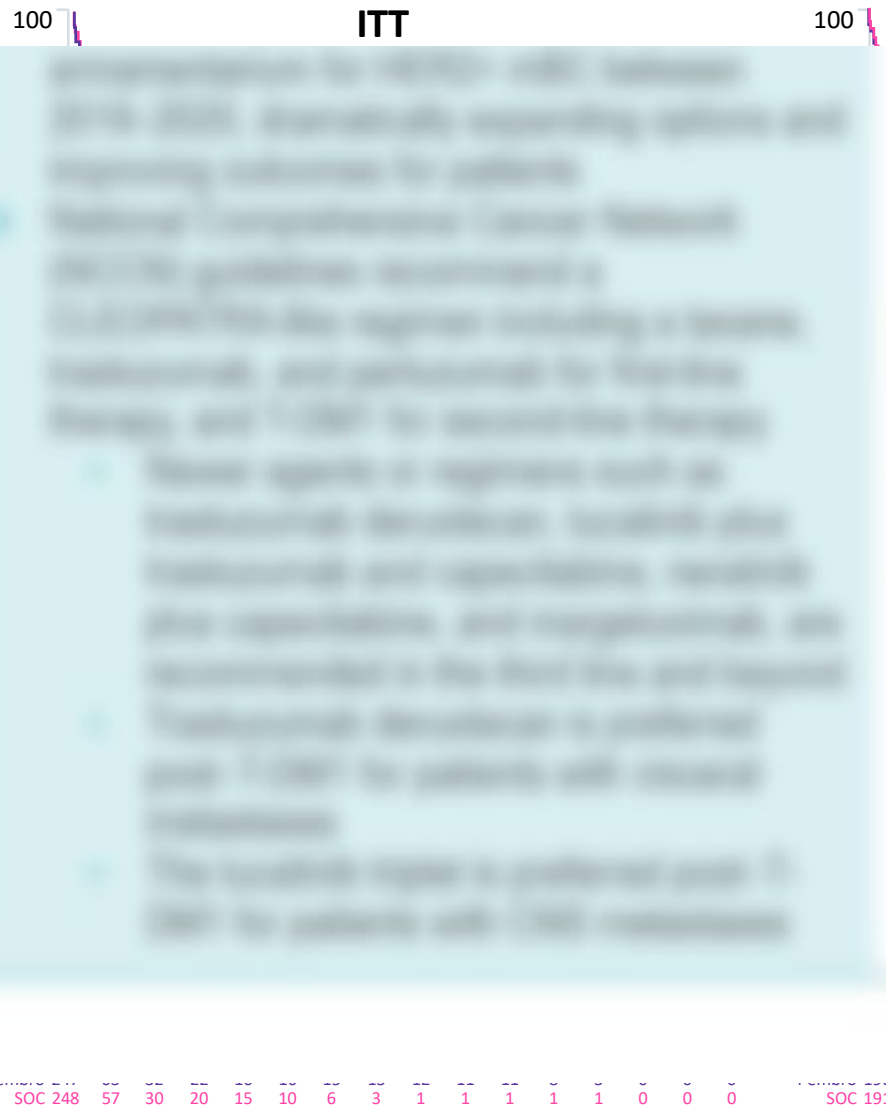
Soulieres et al. ESMO 2022. 658MO

Pembrolizumab (pembro) vs standard-of-care (SOC) in previously treated recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 6-year follow-up of KEYNOTE-040 (2/4)

Soulieres et al. ESMO 2022. 658MO



Data cutoff date: February 3, 2022.

Soulières D, et al. ESMO 2022. Oral presentation.

Pembrolizumab (pembro) vs standard-of-care (SOC) in previously treated recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 6-year follow-up of KEYNOTE-040 (3/4)

Soulieres et al. ESMO 2022. 658MO

Data cutoff date: February 3, 2022.

BICR, blinded independent central review; CI, confidence interval; CR, complete response; ITT, intent-to-treat; NA, not available; NE, non-estimable; ORR, objective response rate; PD, partial disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOC, standard of care.

Soulières D, et al. ESMO 2022. Oral presentation.

Pembrolizumab (pembro) vs standard-of-care (SOC) in previously treated recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 6-year follow-up of KEYNOTE-040 (4/4)

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Soulieres et al. ESMO 2022. 658MO

Pembrolizumab with or without chemotherapy for first-line treatment of recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 5-year results from KEYNOTE-048 (1/2)

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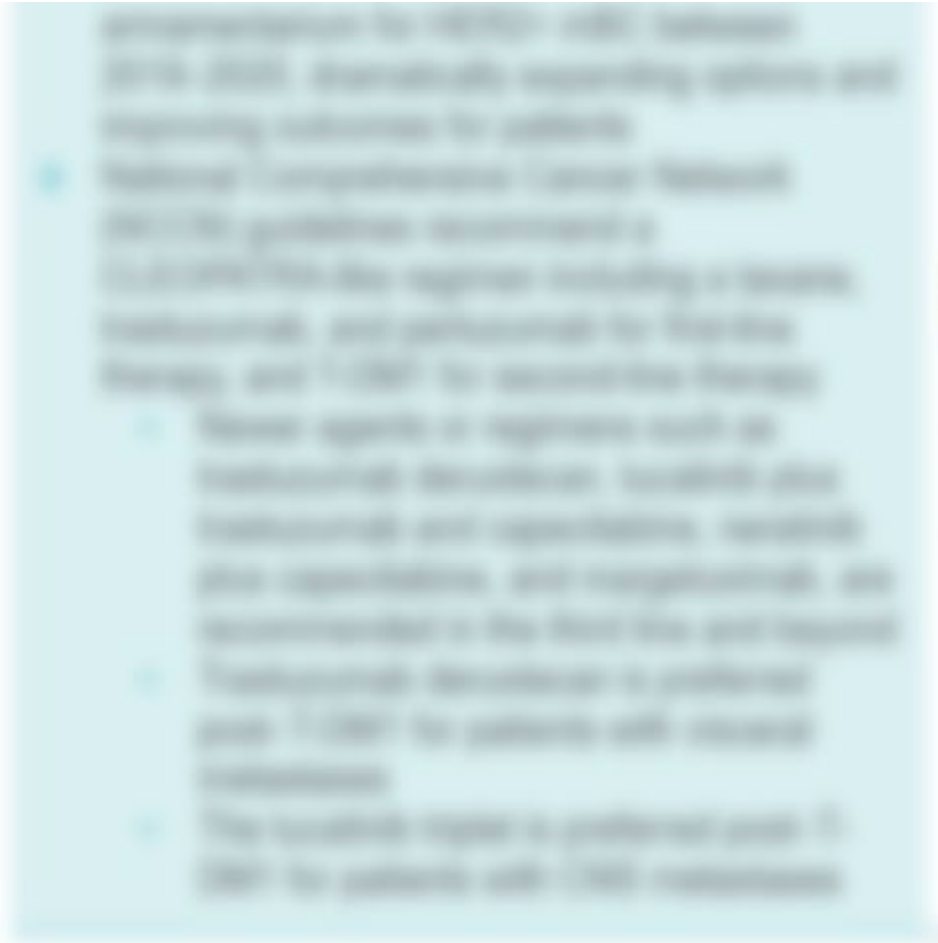
Tahara et al. ESMO 2022. 659MO



Pembrolizumab with or without chemotherapy for first-line treatment of recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): 5-year results from KEYNOTE-048 (2/2)

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Tahara et al. ESMO 2022. 659MO

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Pembrolizumab (pembro) + carboplatin (carbo) + paclitaxel (pacli) as first-line (1L) therapy in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): Phase VI KEYNOTE-B10 study

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Dzienis et al. ESMO 2022. 651O

Effectiveness and quality-of-life (QoL) data from real-world study (ProNiHN) in patients (pts) with recurrent and/or metastatic squamous cell carcinoma of head and neck (R/M SCCHN) treated with nivolumab (nivo) in France

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Le Tourneau et al. ESMO 2022. 695P

HANNA: Real-world data of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN), including first-line population, treated with nivolumab in Germany

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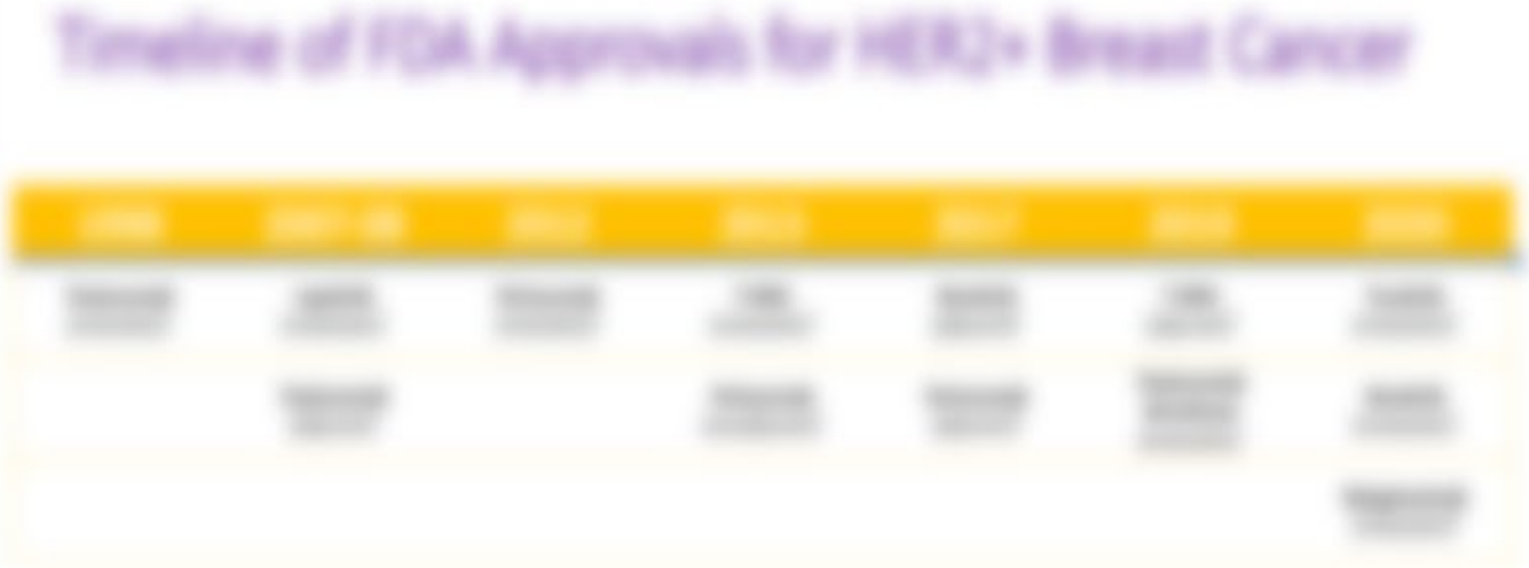
Langer et al. ESMO 2022. 680P



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Immune Checkpoint Inhibitors: Relapsed/Metastatic

Key Takeaways

Key Takeaways: Immune Checkpoint Inhibitors: Relapsed/Metastatic

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- Recently released data are encouraging with regard to improving patient survival in
  - It is a strong prognostic factor for OS and EFS
- The first small-volume (≤3 mL) pull of bone marrow aspirate should be used for MRD quantification
- Flow-based and NGS-based MRD quantification have high correlation for ≥10^{-4} leukemia burden
  - Providers may choose which methodology works best in their practice environment
  - Emerging evidence supports use of NGS with deeper sensitivity
- On the basis of current evidence, serial monitoring of MRD is recommended
- Additional studies are needed to contextualize MRD for different genotypes and to determine optimal, and cost-effective, testing frequency

Discussion Highlight: Immune Checkpoint Therapy Optimization (1/2)

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USE OF CHEMOTHERAPY IN COMBINATION WITH IMMUNOTHERAPY

- It is a strong prognostic factor for OS and EFS

- The first small-volume (≤3 mL) pull of bone marrow aspirate should be used for MRD quantification

- Flow-based and NGS-based MRD quantification have high correlation for ≥10^{-4} leukemia burden
  - Providers may choose which methodology works best in their practice environment
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Discussion Highlight: Immune Checkpoint Therapy Optimization (2/2)

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PEMBROLIZUMAB

- It is a strong prognostic factor for OS and EFS

- The first small volume (≤3 mL) pull of bone marrow aspirate should be used for MRD quantification

- Flow-based and NGS-based MRD quantification have high correlation for ≥10^{-4} leukemia burden
  - Providers may choose which methodology works best in their practice environment
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- On the basis of current evidence, serial monitoring of MRD is recommended

- Additional studies are needed to contextualize MRD for different genotypes and to determine optimal, and cost-effective, testing frequency

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Other Approaches (including investigational IOs)

Andreas Dietz, MD, PhD

University Hospital of Leipzig

Abstracts Covered: Other Approaches (including investigational IOs)

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- 652O – Randomized phase III VANCE study: Gemcitabine and carboplatin (GC)

Randomized phase III VANCE study: Gemcitabine and carboplatin (GC) followed by Epstein Barr virus-specific autologous cytotoxic T lymphocytes (EBV-CTL) vs the same chemotherapy as first-line treatment for advanced nasopharyngeal carcinoma (NPC)

Toh et al. ESMO 2022. 652O

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Phase I study of M6620 (VX-970, berzosertib) in combination with cisplatin and XRT in patients with locally advanced head and neck squamous cell carcinoma

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Bhatia et al. ESMO 2022. 656MO

Early response to leukocyte interleukin Injection (LI) immunotherapy extends overall survival (OS) in locally advanced primary squamous cell carcinoma of the head & neck (SCCHN): The IT-MATTERS study

Lavin et al. ESMO 2022. 690P

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OPTIM: A randomized phase II study on the OPTimization of IMmunotherapy in squamous carcinoma of the head and neck – AIO-KHT-0117

Gruenwald et al. ESMO 2022. 681P

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A phase II trial of pembrolizumab and cabozantinib in pts with recurrent metastatic head and neck SCC

Saba et al. ASCO 2022 6008

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Other Approaches (including investigational IOs)

Key Takeaways

Key Takeaways: Other Approaches (including investigational IOs)

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> The experts positively view attempts to test new MOAs to move the field forward

Discussion Highlight: Immune Checkpoint Therapy Optimization

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KINASE INHIBITORS

STUDY POPULATION

- MEDALIST study: MDS patients with ≤10% ring sideroblasts or ≤5% with *SF3B1* mutation, <5% blasts in bone marrow, non-del(5q) MDS, refractory/intolerant to ESAs, or naive, average RBC transfusion burden ≥2 U/8 weeks, no prior treatment with disease-modifying agents (eg, IMiDs, HMAIs); randomized to luspatercept (n = 153) or placebo (n = 76). This subanalysis: 96/153 patients who did not achieve RBC transfusion independence (TI) for ≥8 weeks by week 23 but continued treatment through week 48

OUTCOMES

- 56% (n = 71/96) of patients achieved RBC TI for ≥8 weeks
  - 24 hours, 1 patients achieved RBC TI for ≥24 weeks
  - Median time to achieving RBC TI for ≥8 weeks was 3 months

EXPERT CONCLUSIONS

Continuing luspatercept treatment beyond week 23 provides clinical benefit in late responders and decreases the transfusion load in patients