

# Practical Management Pearls for Immunotherapy for the Treatment of Head and Neck Squamous Cell Carcinoma

January 13, 2021

12:30 – 1:30 p.m. EST

# Webinar moderators



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

Expert Panel Chair



**Nancy Y. Lee, MD –**  
*Memorial Sloan Kettering  
Cancer Center*

# Webinar presenters



**Barbara A. Burtness,  
MD** – *Yale University  
School of Medicine*



**Lisa Licitra, MD** –  
*Fondazione IRCCS Istituto  
Nazionale dei Tumori*



**Kevin J. Harrington,  
MBBS, PhD** – *The Institute  
of Cancer Research*



**Rebecca L. Lewis, CRNP** –  
*UPMC Hillman Cancer  
Center*

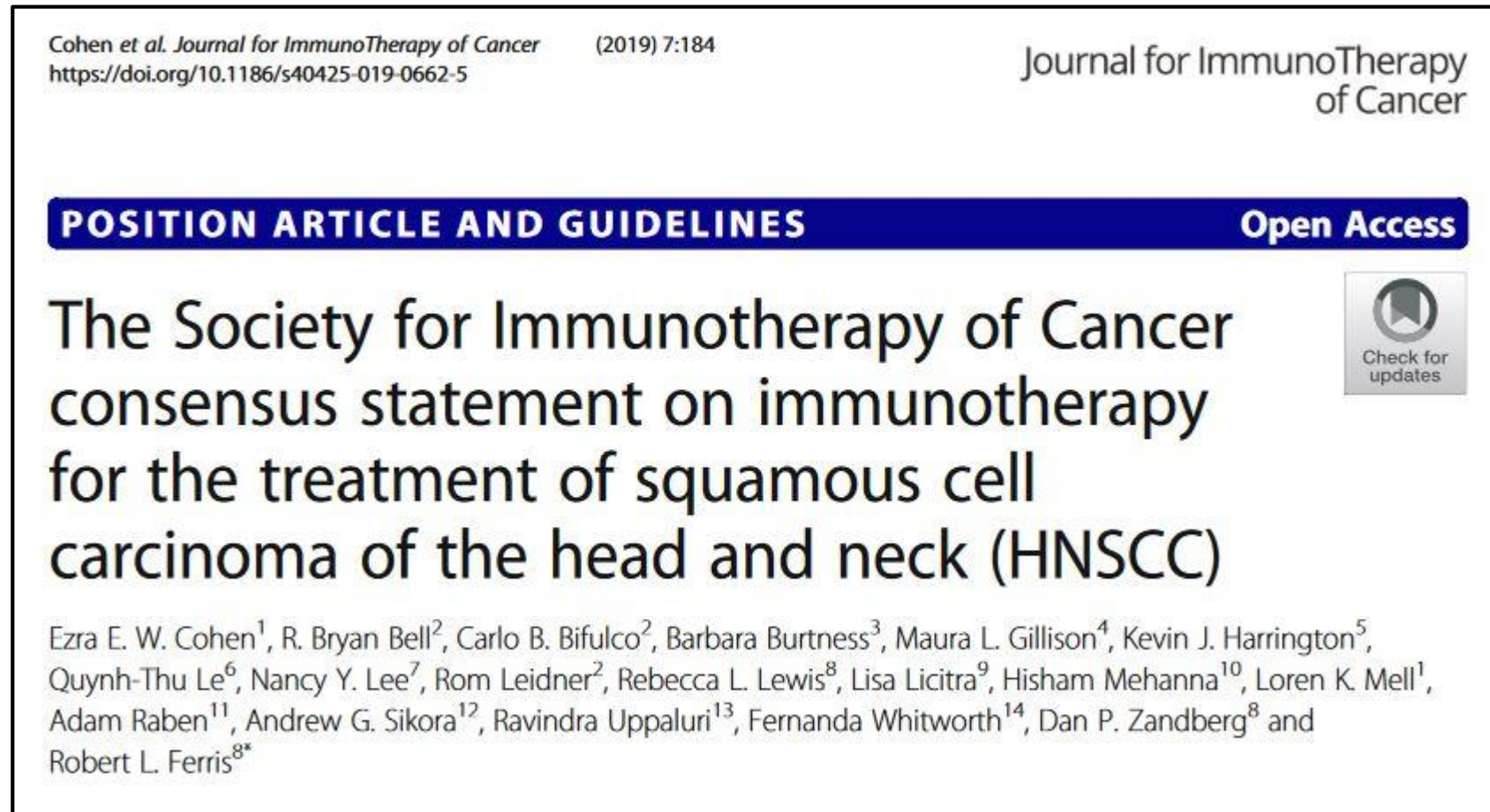
# Learning objectives

- Identify and incorporate head/neck-specific considerations into the use of immunotherapy
- Determine optimal sequencing and duration of immunotherapy
- Determine optimal monitoring strategies to detect toxicity and disease response
- Appropriately manage toxicities/irAEs associated with immunotherapy of head/neck cancers

# Webinar outline

- Development of the guideline
- Biomarkers (*Dr. Burtness*)
- Initiation, response monitoring and discontinuation of immunotherapy (*Dr. Licitra*)
- Immunotherapy sequencing (*Dr. Harrington*)
- Management of immune-related adverse events (*Dr. Licitra and Ms. Lewis*)
- Key takeaways

# Development of the guideline



# Development of the guideline

- Developed according to the Institute of Medicine's Standards for Developing Trustworthy Clinical Practice Guidelines
- Panel consisted of 19 experts in the field
- Recommendations are based upon published literature evidence, or clinical evidence where appropriate
- Consensus was defined at 75% approval among voting members

# Webinar outline

- Development of the guideline
- **Biomarkers (*Dr. Burtness*)**
- Initiation, response monitoring and discontinuation of immunotherapy
- Immunotherapy sequencing
- Management of immune-related adverse events
- Key takeaways

# Biomarkers

## Expert Panel recommendations\*:

- *94% of the Expert Panel defined positivity for PD-L1 as  $\geq 1\%$  TPS or  $\geq 1$  CPS by IHC staining. However, it is important to note that expression levels may differ depending on the antibody used and whether staining includes tumor alone (TPS) or tumor plus stroma (CPS). The majority of the Expert Panel (81%) also agreed that the best use of biomarker testing when treating patients with HNSCC with immunotherapy is by combined positive score (CPS).*
- *HPV status should not affect selection of patients with platinum-refractory R/M HNSCC for ICI therapy. 55.5% of the Expert Panel stated that HPV status (based on p16 overexpression) should be included in treatment planning.*
- *Given the low rate of MSI incidence in HNSCC, the Expert Panel (88%) recommended against standard MSI testing, unless the patient is having a genome profile performed already which will provide such information.*

\*Guideline published July 15, 2019.

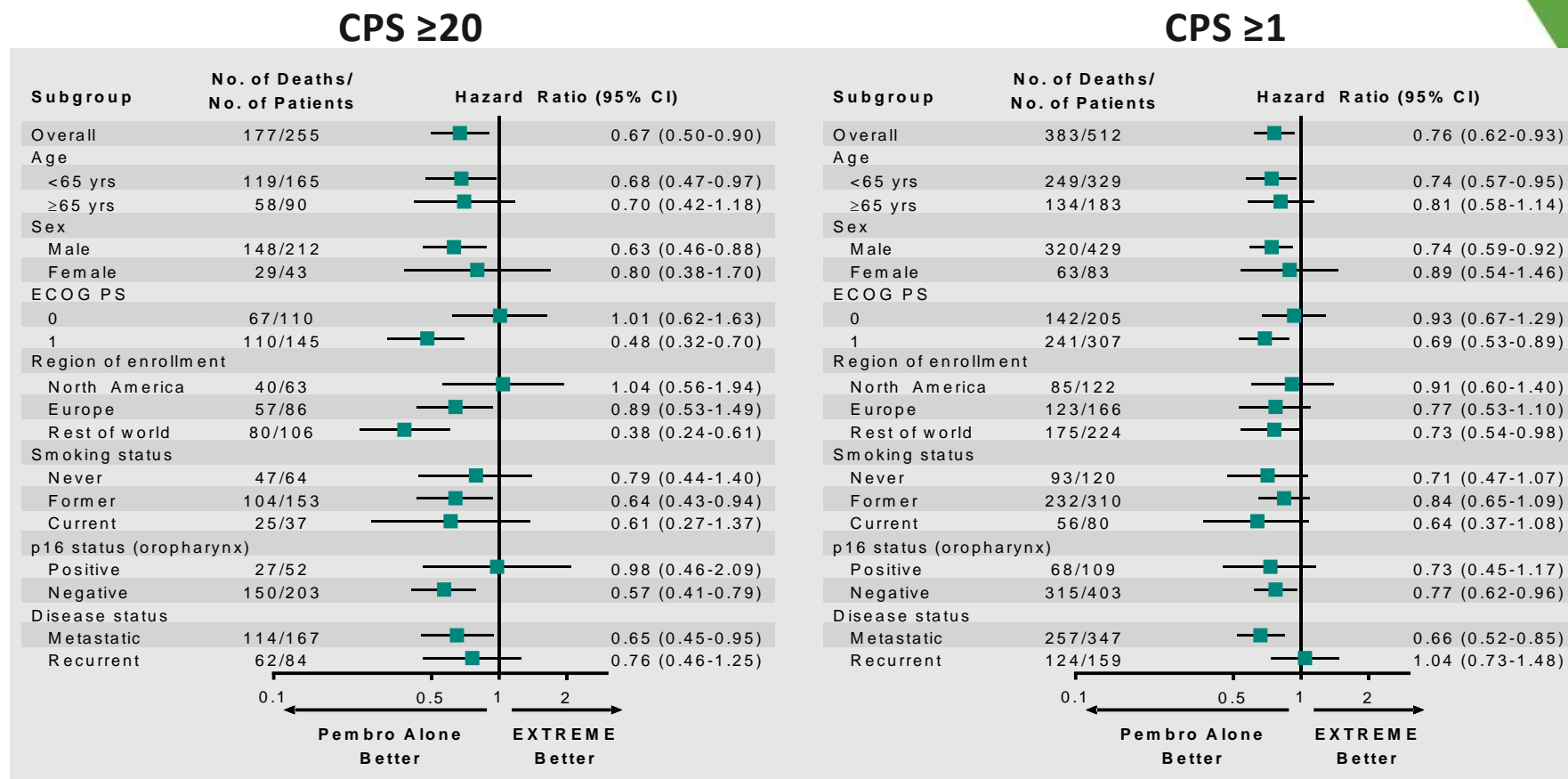
# Biomarkers

- PD-L1 testing
  - Necessity of PD-L1 testing
  - PD-L1-low disease
  - Which assay to use for PD-L1-based indications
    - 28-8, 22C3, in-house assays
    - TPS vs. CPS
- Practical considerations for PD-L1 testing
  - Quantification of PD-L1 result
  - CPS vs TPS
  - Implications for CPS  $\geq 20$

# Other considerations

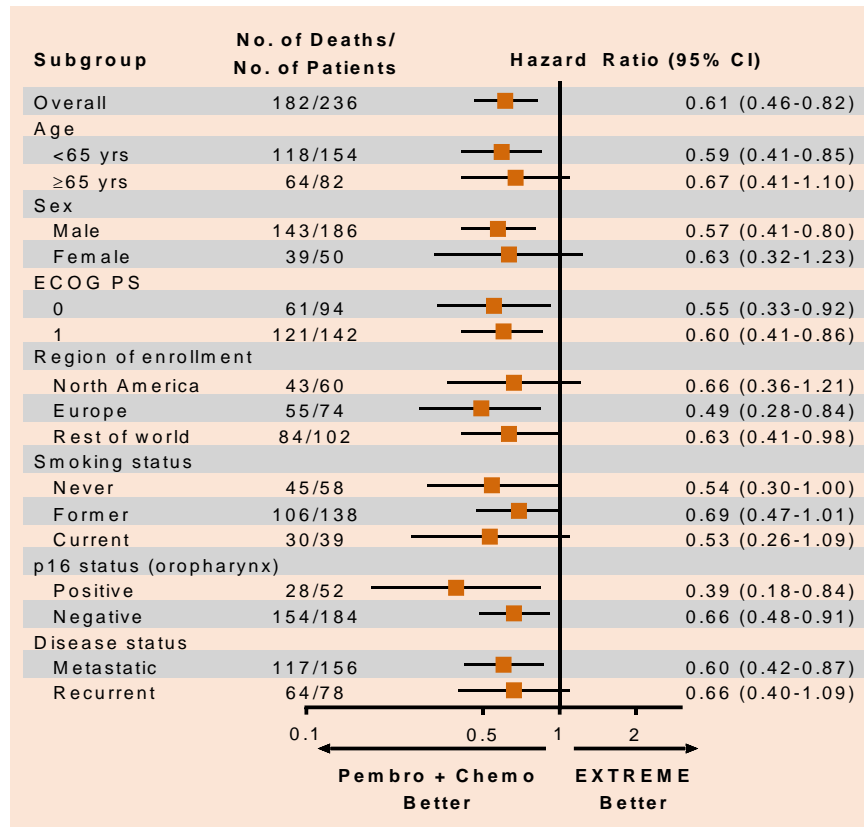
- Presence/absence of symptoms, pace of disease
- TMB/MSI testing and implications for treating PD-L1 negative disease
  - IFN-g-related gene expression signatures
  - Implications from EAGLE study

# Overall Survival in Pembrolizumab vs. EXTREME

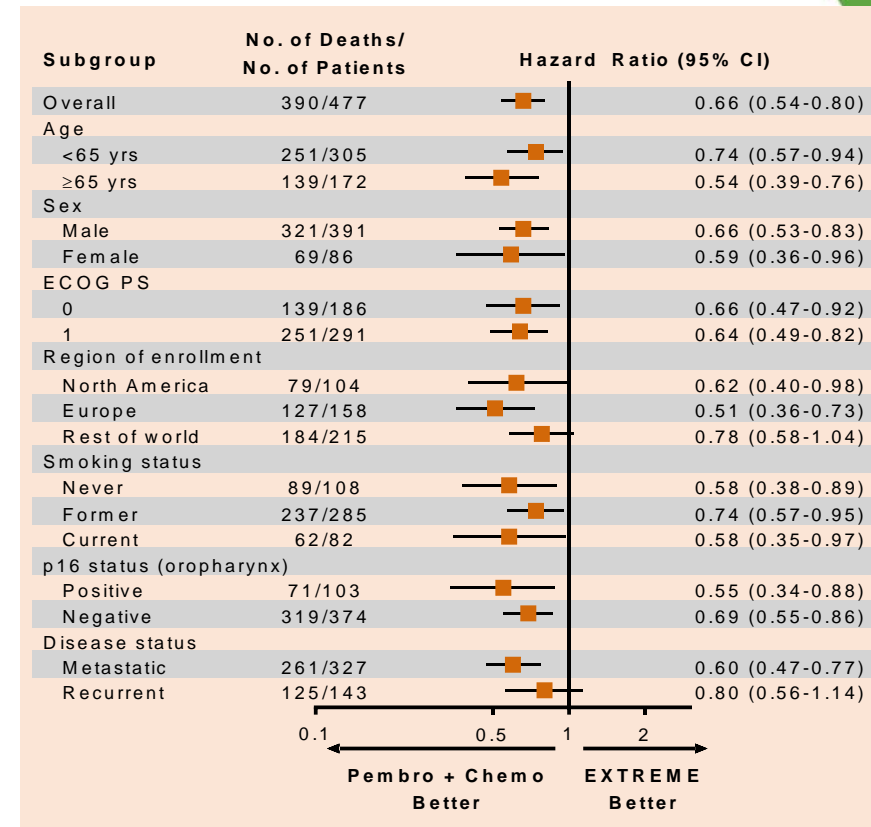


# OS in Subgroups, P+C vs E

CPS ≥20



CPS ≥1



# Implications in HPV-Associated Disease

- May be indolent and oligometastatic disease
- Desire to minimize toxicity
- Weighed against chemosensitivity of these cancers and strong HR in favor of pembrolizumab/chemotherapy compared with cetuximab/chemotherapy

# Webinar outline

- Development of the guideline
- Biomarkers
- Initiation, response monitoring and discontinuation of immunotherapy (*Dr. Licitra*)
- Immunotherapy sequencing
- Management of immune-related adverse events
- Key takeaways

# Eligibility for ICI therapy

## Expert Panel recommendations\*:

- *Do NOT automatically disqualify patient for anti-PD-1 immunotherapy based on: age (89% Expert Panel agreement), lung metastases (89% Expert Panel agreement) or co-morbidities (75% Expert Panel agreement). Additionally, the Expert Panel agrees (81%) that patients with autoimmune disease should not automatically be excluded but rather, the decision should be tailored to the specific disease*
- *Patients who have controlled diseases such as Hepatitis C or who are HIV+ with normal CD4+ T cell counts and who are on antiretroviral therapy are generally suitable for ICI treatment. (75% Expert Panel agreement)*
- *While 55.5% of the Expert Panel stated that HPV status (based on p16 overexpression) should be included in treatment planning, 83% voted that it does not influence their decision to treat patients with R/M HNSCC with standard of care immunotherapy.*

*\*Guideline published July 15, 2019. Recommendations since updated.*

# Additional considerations for determining ICI eligibility

- Patients who are HCV<sup>+</sup> or HIV<sup>+</sup>
  - ICI for treatment of HIV-related conditions
  - Updated practices from NCI
- Patients with significant disease burden or fast-paced disease
  - Favoring chemotherapy in patients with high disease burden
  - Postponing progression in patients with hyperprogressive or progressive disease
- Patients requiring immunosuppressive medications
- Patients requiring antibiotics

# Response monitoring

## Expert Panel recommendations\*:

- *For initial assessment, the Expert Panel recommends using either a CT (53%) or PET-CT (41%) scan following a baseline clinical exam of the patient. To best capture the dynamics of changing tumor size, the Expert Panel recommends imaging, particularly utilizing a CT scan (44%).*
- *In monitoring patients for signs of response after initial follow-up, the majority of the Expert Panel (65%) recommends patient evaluation (via radiographic imaging) every three months with SOC imaging to be adapted to patient disease status, response, and tolerability of the regimen.*
- *In the event radiographic progression is observed early in treatment, and the patient is clinically stable, the majority of the Expert Panel (76%) recommends continuing immunotherapy treatment until progression is confirmed on a second scan. The recommendation to continue immunotherapy until a second scan confirms progression may be modified depending on clinical trial options available for 2nd or 3rd line treatment as well as the specific characteristics and kinetics of the patient's disease such as PD-L1 expression, prior therapies, disease burden, or rapid progression with high symptom burden*

*\*Guideline published July 15, 2019. Recommendations since updated.*

# Additional considerations for response monitoring/imaging

- Frequency – spacing out imaging more once pts are in CR
- CT versus PET-CT
  - dependent on disease site, volume of change
  - PET-CT used less frequently, especially early in therapy; often denied by insurance

# Immunotherapy discontinuation following a (near-)complete response

Expert Panel recommendations\*:

- *In determining duration of treatment in the case of a patient experiencing a CR or near CR after treatment with anti-PD1 therapy, 53% of the Expert Panel recommend continuing treatment for at least two years (up to indefinitely) or until the patient experiences disease progression or toxicity*

*\*Guideline published July 15, 2019. Recommendations since updated.*

# Webinar outline

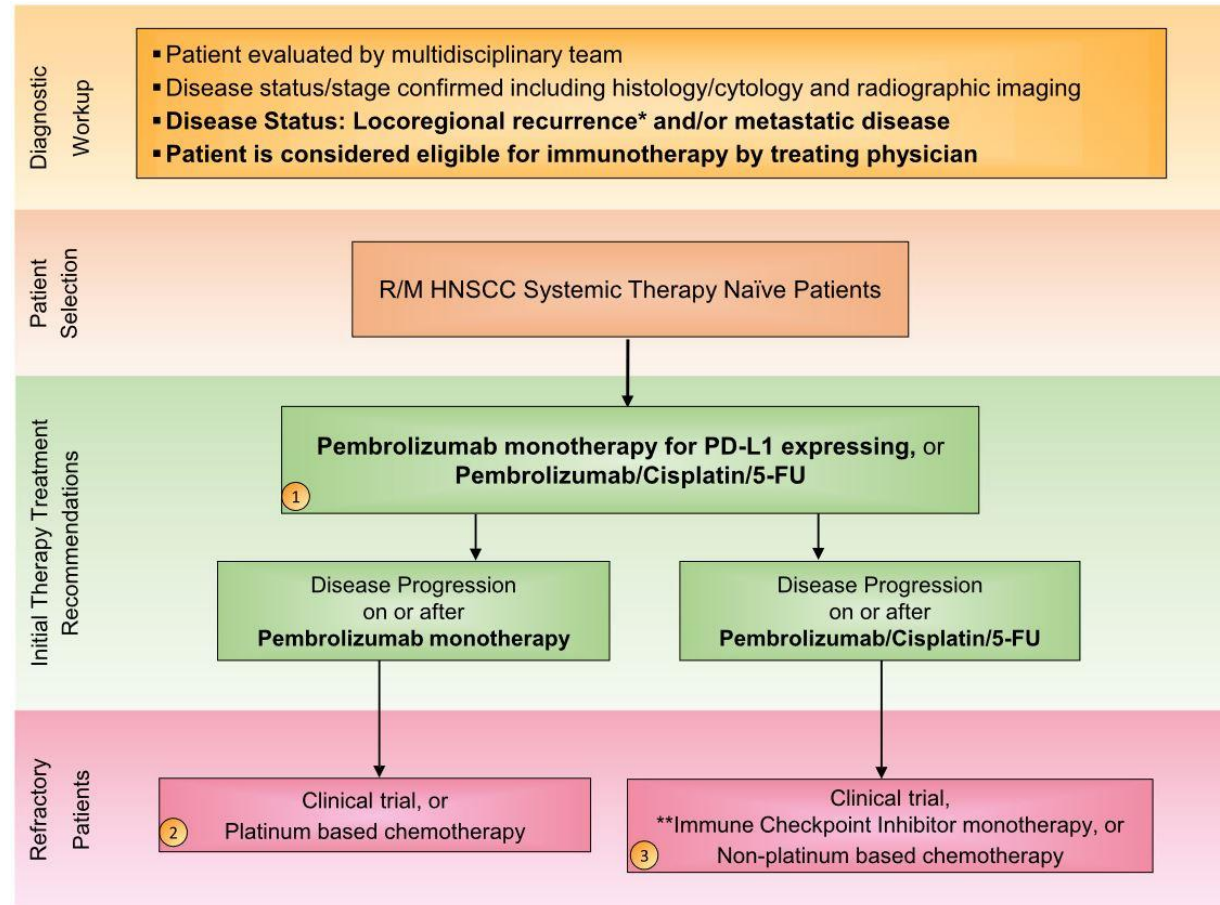
- Development of the guideline
- Biomarkers
- Initiation, response monitoring and discontinuation of immunotherapy
- Immunotherapy sequencing (*Dr. Harrington*)
- Management of immune-related adverse events
- Key takeaways

# First-line treatment

Expert Panel recommendations\*:

- Pembrolizumab is indicated for treatment-naïve R/M HNSCC. (Category 1)
  - Pembrolizumab monotherapy may be used to treat patients with treatment naïve R/M HNSCC and PD-L1 CPS  $\geq 1$ . (Category 1)
  - Pembrolizumab + chemotherapy (platinum and fluorouracil (FU)) may be used to treat all patients with treatment naïve, biomarker-unspecified R/M HNSCC patients. (Category 1)

# First-line treatment algorithm for R/M HNSCC patients\*



\*Subject to jurisdiction-specific variations

Diagnostic  
Workup

- Patient evaluated by multidisciplinary team
- Disease status/stage confirmed including histology/cytology and radiographic imaging
- **Disease Status: Locoregional recurrence\* and/or metastatic disease**
- **Patient is considered eligible for immunotherapy by treating physician**

Patient  
Selection

R/M HNSCC Systemic Therapy Naïve Patients

Initial Therapy Treatment  
Recommendations

**Pembrolizumab monotherapy for PD-L1 expressing, or  
Pembrolizumab/Cisplatin/5-FU**

Disease Progression  
on or after  
**Pembrolizumab monotherapy**

Disease Progression  
on or after  
**Pembrolizumab/Cisplatin/5-FU**

Refractory  
Patients

Clinical trial, or  
Platinum based chemotherapy

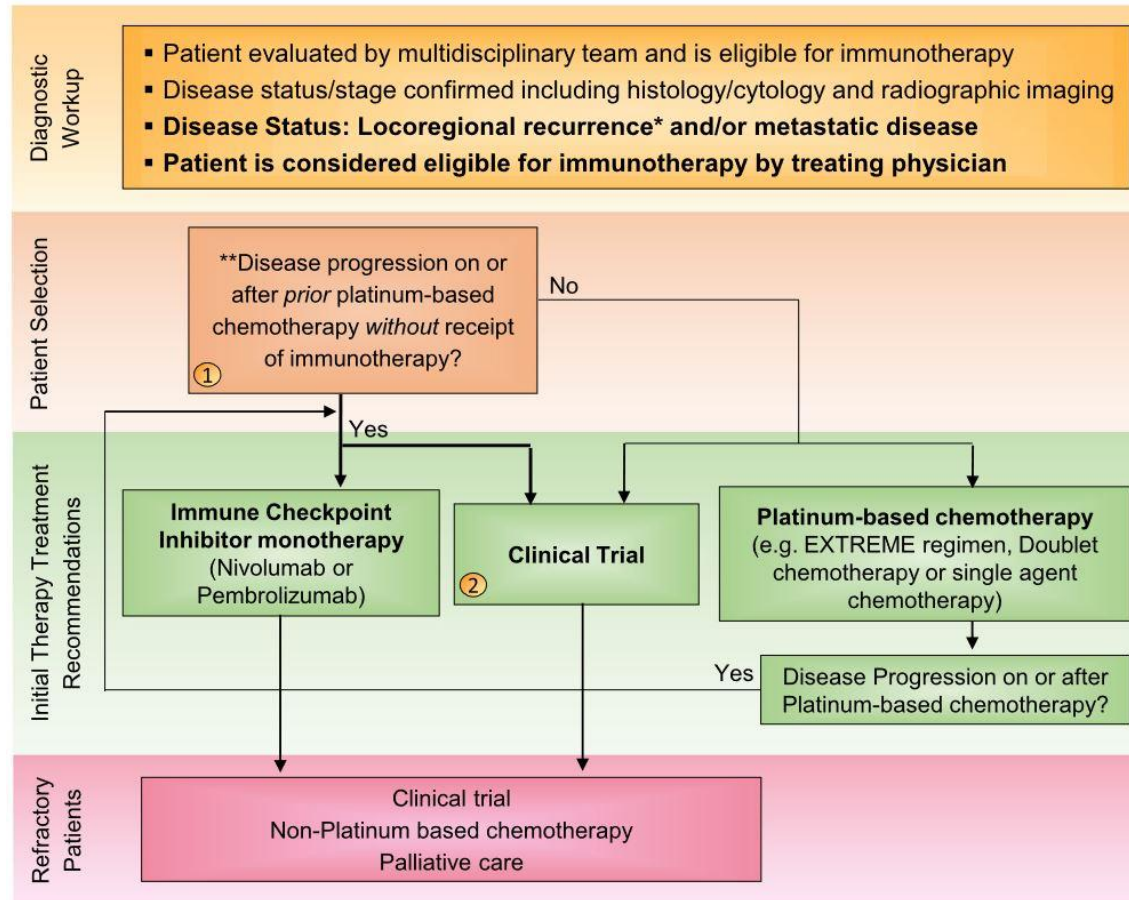
Clinical trial,  
\*\*Immune Checkpoint Inhibitor monotherapy, or  
Non-platinum based chemotherapy

# Second-line treatment for platinum-refractory patients

Expert Panel recommendations\*:

- *Pembrolizumab or nivolumab monotherapy should be used to treat patients with R/M HNSCC who are platinum-refractory, including those that progressed within six months of platinum-based chemotherapy. (Category 1)*
- *If a clinical trial is available, the majority of the Expert Panel (94%) found this to be the preferred option, especially if it is a biomarker-based, hypothesis-driven clinical trial (59%).*

# Second-line treatment algorithm for R/M HNSCC patients



Diagnostic  
Workup

- Patient evaluated by multidisciplinary team and is eligible for immunotherapy
- Disease status/stage confirmed including histology/cytology and radiographic imaging
- **Disease Status: Locoregional recurrence\* and/or metastatic disease**
- **Patient is considered eligible for immunotherapy by treating physician**

Patient Selection

①  
\*\*Disease progression on or  
after *prior* platinum-based  
chemotherapy *without* receipt  
of immunotherapy?

No

Yes

Initial Therapy Treatment  
Recommendations

**Immune Checkpoint  
Inhibitor monotherapy**  
(Nivolumab or  
Pembrolizumab)

②  
**Clinical Trial**

**Platinum-based chemotherapy**  
(e.g. EXTREME regimen, Doublet  
chemotherapy or single agent  
chemotherapy)

Yes

Disease Progression on or after  
Platinum-based chemotherapy?

Refractory  
Patients

Clinical trial  
Non-Platinum based chemotherapy  
Palliative care

# Additional considerations for immunotherapy sequencing

- Treatment following progression on first-line immunotherapy
- Emerging data for **NPC therapy**
  - pembrolizumab, nivolumab – Category 2B as “subsequent-line” in NCCN 2021
  - toripalimab [JUPITER-02 study]
  - camrelizumab [CAPTAIN-1<sup>st</sup> study]
  - tislelizumab [RATIONALE-309 study]
  - what to offer while awaiting approval?

# *Panel Discussion*

- **CheckMate 651**
  - Limitations
  - PFS in control arm high (de novo more favorable)
- **EAGLE**
- **JAVELIN**

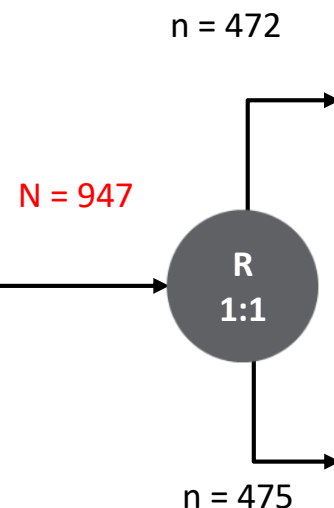
# CheckMate 651 study design

## Key eligibility criteria

- R/M SCCHN (oral cavity, oropharynx, hypopharynx, or larynx)
- No prior treatment for R/M disease
- Prior chemotherapy for LAD permitted if progression-free ≥6 months post-treatment
- ECOG PS 0–1

## Stratified by:

p16 expression (OPC p16+ vs p16–/non-OPC)  
Tumor PD-L1<sup>a</sup> status (<1% vs ≥1%)  
Prior chemotherapy (yes vs no)



**NIVO 3 mg/kg Q2W  
+  
IPI 1 mg/kg Q6W**

## EXTREME regimen<sup>b</sup>

Cetuximab + cisplatin/carboplatin + 5-FU  
Q3W for 6 cycles followed by  
cetuximab<sup>c</sup> monotherapy Q1W

Until disease progression,  
unacceptable toxicity,  
or 2 years for  
NIVO + IPI

## Primary endpoints (independently tested)

- OS in all randomized
- OS in PD-L1 CPS<sup>a</sup> ≥20

## Secondary endpoints

- OS in PD-L1 CPS ≥1<sup>d</sup>
- PFS by BICR (all randomized, PD-L1 CPS ≥20)
- ORR/DOR by BICR (all randomized, PD-L1 CPS ≥20)

## Exploratory endpoints

- PFS and ORR/DOR in PD-L1 CPS ≥1
- Patient-reported outcomes
- Safety

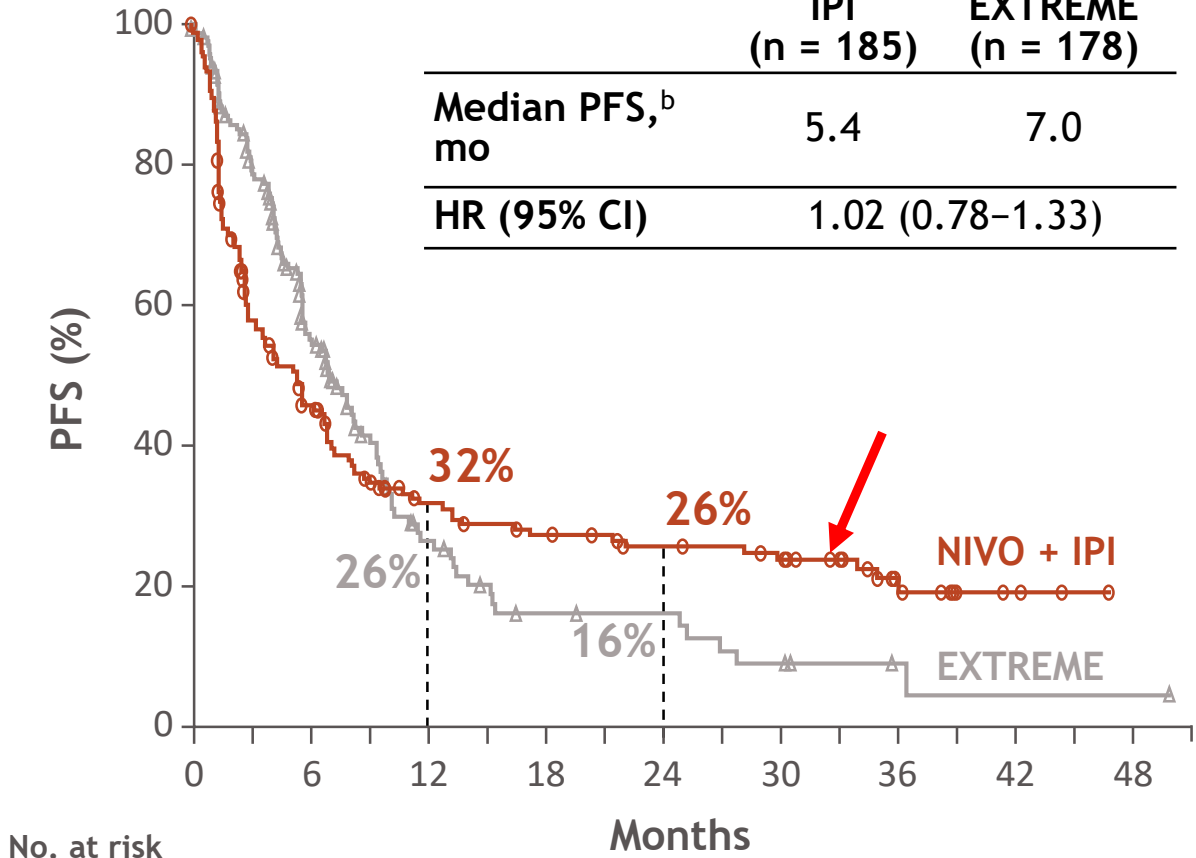
NCT02741570. Database lock: June 21, 2021; minimum / median follow-up: 27.3 months / 39.1 months.

<sup>a</sup>Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); <sup>b</sup>Initial cetuximab dose of 400 mg/m<sup>2</sup> once only, then cetuximab 250 mg/m<sup>2</sup> Q1W plus cisplatin 100 mg/m<sup>2</sup> or carboplatin AUC 5 on day 1, plus fluorouracil 1000 mg/m<sup>2</sup>/d for 4 days for 6 cycles (Q3W); <sup>c</sup>Cetuximab 250 mg/m<sup>2</sup> Q1W; Q2W maintenance was allowed per local prescribing information; <sup>d</sup>Part of statistical testing hierarchy. BICR, blinded independent central review; CPS, combined positive score; DOR, duration of response; LAD, locally advanced disease; OPC, oropharyngeal cancer; ORR, objective response rate.

# Efficacy in PD-L1 CPS ≥20 population

## PFS<sup>a</sup>

	NIVO + IPI (n = 185)	EXTREME (n = 178)
Median PFS, <sup>b</sup> mo	5.4	7.0
HR (95% CI)	1.02 (0.78–1.33)	



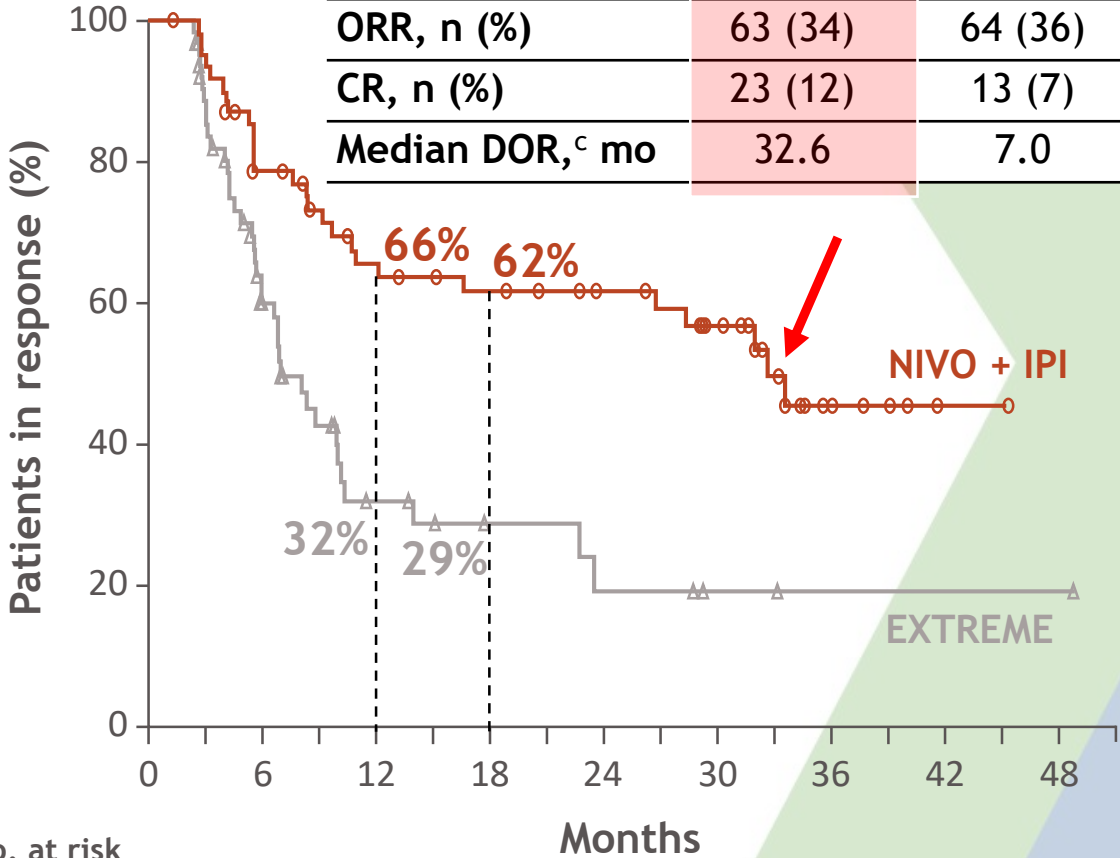
No. at risk	Months	0	6	12	18	24	30	36	42	48
NIVO + IPI	185	73	43	35	29	25	11	4	0	0
EXTREME	178	70	22	10	9	5	2	1	1	0

Minimum follow-up: 27.3 months.

<sup>a</sup>Per BICR; <sup>b</sup>95% CI = 3.1–6.9 (NIVO + IPI) and 5.6–8.7 (EXTREME); <sup>c</sup>95% CI = 12.1–NR (NIVO + IPI) and 5.6–10.1 (EXTREME). BICR, blinded independent central review; CR, complete response; DOR, duration of response; ORR, objective response rate.

## ORR<sup>a</sup> and DOR<sup>a</sup>

	NIVO + IPI (n = 185)	EXTREME (n = 178)
ORR, n (%)	63 (34)	64 (36)
CR, n (%)	23 (12)	13 (7)
Median DOR, <sup>c</sup> mo	32.6	7.0



No. at risk	Months	0	6	12	18	24	30	36	42	48
NIVO + IPI	63	46	34	30	26	20	7	2	0	0
EXTREME	64	30	11	6	4	2	1	1	1	0

# EAGLE: A Phase 3, Randomized, Open-Label Study of Durvalumab (D) With or Without Tremelimumab (T) in Patients With Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (R/M HNSCC)

Lisa Licitra,<sup>1</sup> Robert Haddad,<sup>2</sup> Caroline Even,<sup>3</sup> Makoto Tahara,<sup>4</sup> Mikhail Dvorkin,<sup>5</sup> Tudor-Eliade Ciuleanu,<sup>6</sup> Paul Clement,<sup>7</sup> Ricard Mesia,<sup>8</sup> Svetlana Kutukova,<sup>9</sup> Lyubov Zholudeva,<sup>10</sup> Amaury Daste,<sup>11</sup> Javier Caballero Daroqui,<sup>12</sup> Bhumsuk Keam,<sup>13</sup> Ihor Vynnychenko,<sup>14</sup> Cedrik Lafond,<sup>15</sup> Jagdish Shetty,<sup>16</sup> Nassim Morsli,<sup>17</sup> Helen Mann,<sup>17</sup> Jérôme Fayette,<sup>18</sup> Robert L Ferris<sup>19</sup>

<sup>1</sup>Fondazione IRCCS Istituto Tumori, Milan and the University of Milan, Milan, Italy; <sup>2</sup>Dana Farber Cancer Institute, Boston, MA; <sup>3</sup>Institut Gustave Roussy, Villejuif, France; <sup>4</sup>National Cancer Center Hospital East, Kashiwa, Japan; <sup>5</sup>Omsk Regional Oncology Dispensary, Omsk, Omskaya, Russian Federation; <sup>6</sup>Institute of Oncology/University of Medicine and Pharmacy, Cluj-Napoca, Romania; <sup>7</sup>Leuven Cancer Institute, KU Leuven, Belgium; <sup>8</sup>Barcelona University, Barcelona, Spain; <sup>9</sup>City Clinical Oncology Dispensary, Saint Petersburg, Russian Federation; <sup>10</sup>Regional Transcarpathian Oncological Dispensary, Uzhgorod, Ukraine; <sup>11</sup>Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; <sup>12</sup>Hospital Universitario La Fe, Valencia, Spain; <sup>13</sup>Seoul National University, Seoul, Republic of Korea; <sup>14</sup>Sumy State University, Sumy Regional Oncology Center, Sumy, Ukraine; <sup>15</sup>Clinique Victor Hugo Le Mans, Le Mans, France; <sup>16</sup>AstraZeneca, Gaithersburg, MD; <sup>17</sup>AstraZeneca, Cambridge, United Kingdom; <sup>18</sup>Centre Léon Bérard, Lyon, France; <sup>19</sup>UPMC Hillman Cancer Center, Pittsburgh, PA

# EAGLE: Phase 3 Trial of D and D+T as 2L Treatment of HNSCC

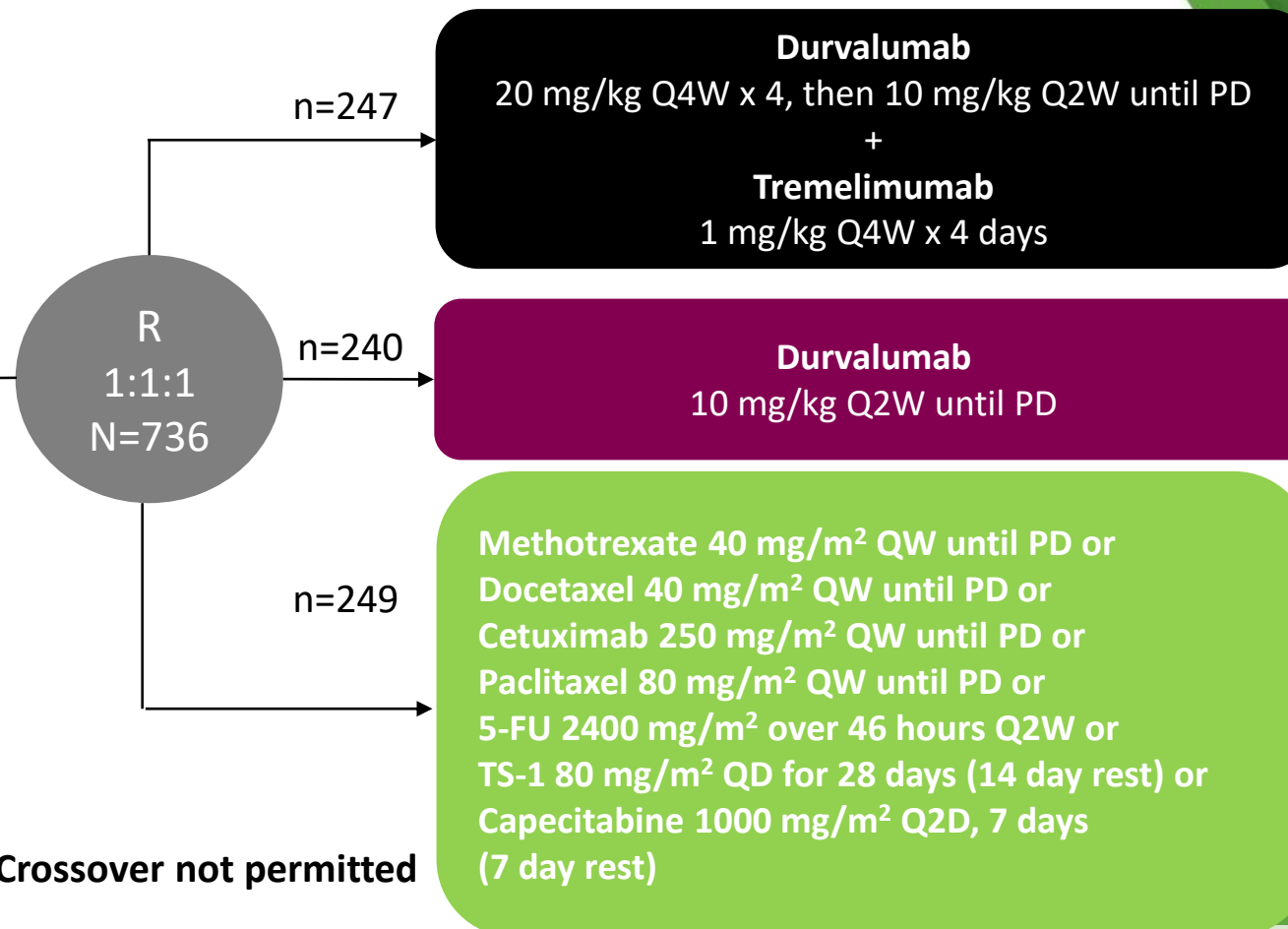
## Key eligibility criteria

- SCC of the oral cavity, oropharynx, hypopharynx, or larynx
- PD after platinum-containing regimen for R/M HNSCC or recurrence within 6 months of multimodal therapy using platinum with curative intent
- ECOG PS 0 or 1
- Known HPV status (oropharynx)
- Tissue sample for PD-L1 assessment

## Stratification factors

- PD-L1 status (TC  $\geq 25\%$  vs  $< 25\%$ )
- Tumor location/HPV status (OPC HPV– vs HPV+ vs non-OPC)
- Smoking history ( $< 10$  vs  $> 10$  pack/y)

**Crossover not permitted**



## 1° Endpoint:

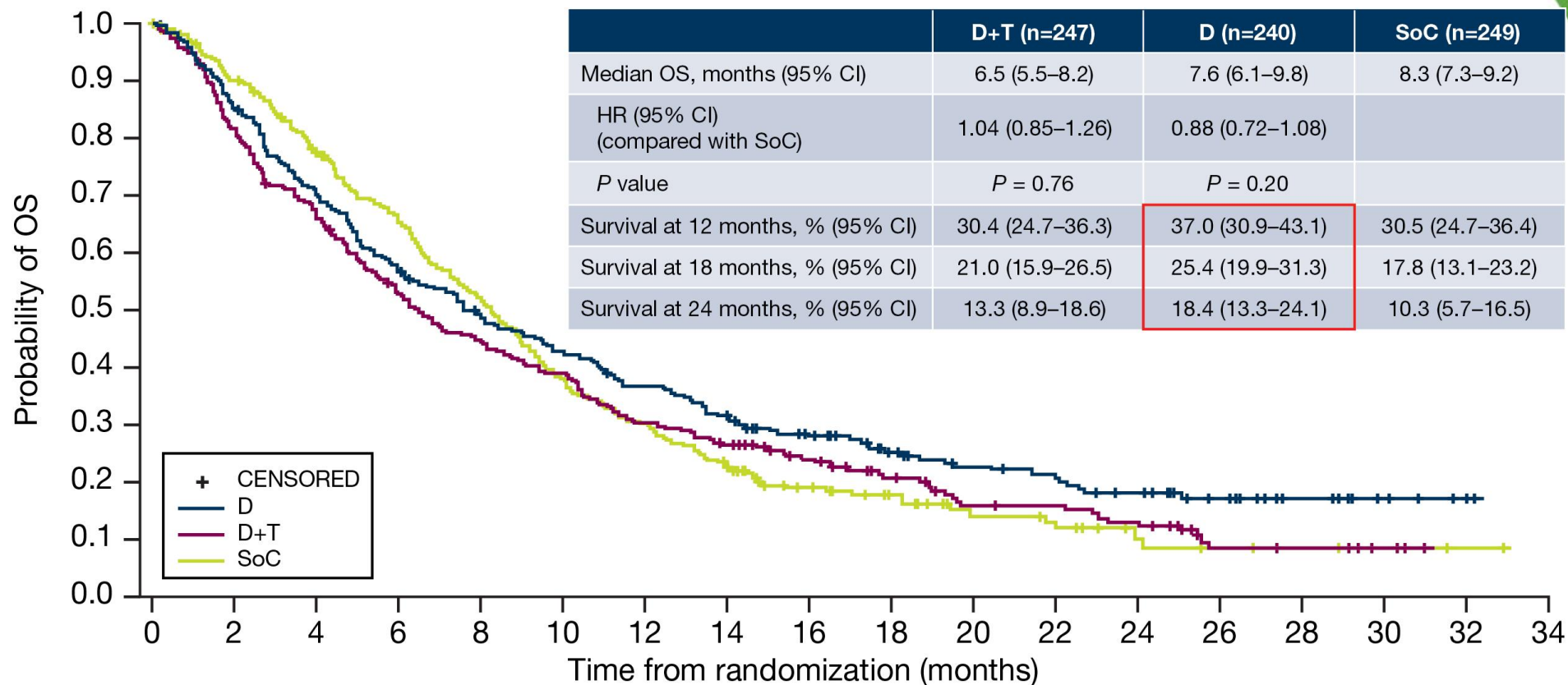
- OS

## 2° Endpoints:

- PFS, ORR, DoR, DCR, OS12
- HRQoL
- Safety
- Biomarkers

2L, second line; 5-FU, 5-fluorouracil; D, durvalumab; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HPV, human papillomavirus; HRQoL, health-related quality of life; mo, month; OPC, oropharyngeal cancer; ORR, objective response rate; OS, overall survival; OS12, overall survival at 12 months; PD, progressive disease; PD-L1, programmed death ligand-1; PFS, progression-free survival; qd, every day; qw, every week; R/M HNSCC, recurrent/metastatic head and neck squamous cell carcinoma; SCC, squamous cell carcinoma; TC, tumor cell; T, tremelimumab; TS-1, tegafur/gimeracil/oteracil.

# EAGLE: OS by Treatment Arm (ITT Population)



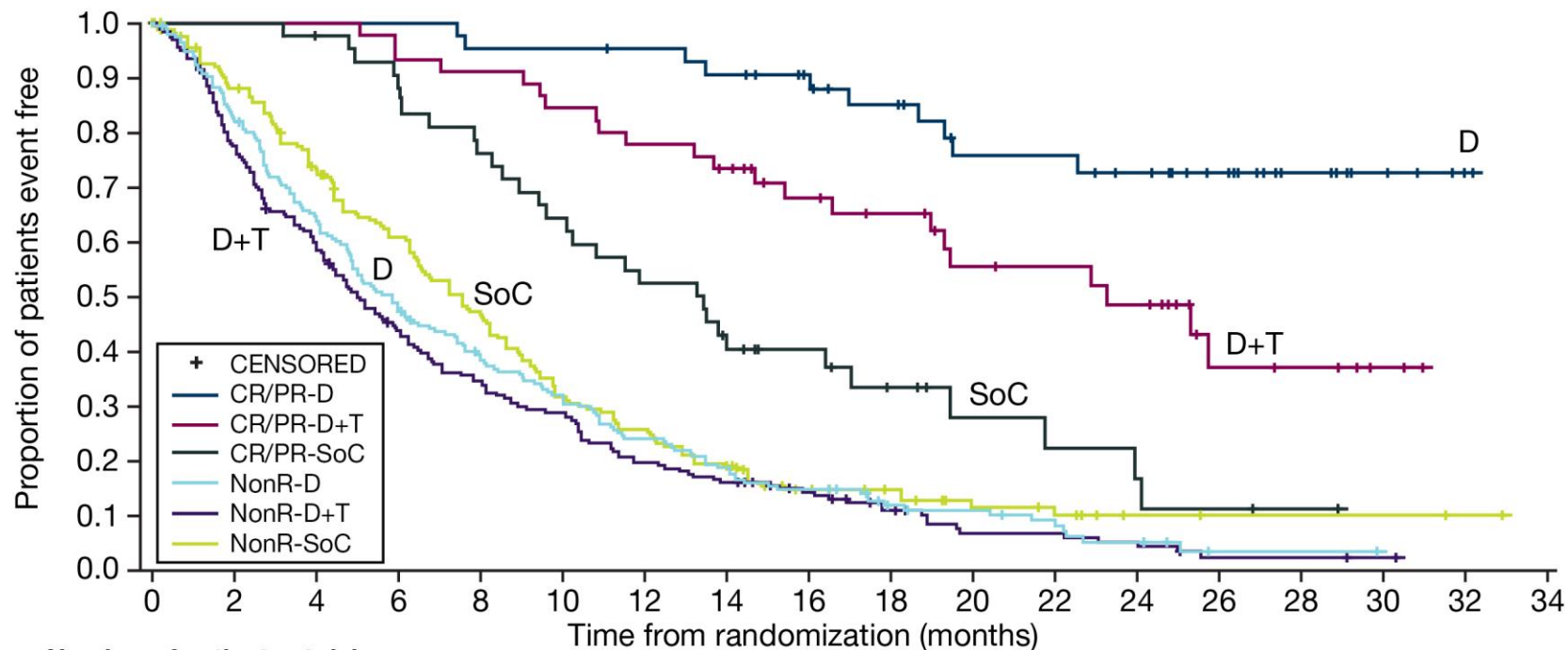
## Number of patients at risk

D	240	205	169	138	115	100	85	73	59	44	36	33	26	17	10	5	2	0
D+T	247	200	165	127	108	94	73	63	48	37	25	24	20	8	7	3	0	0
SoC	249	219	186	154	122	89	71	53	32	23	14	12	6	4	3	2	1	0

- Primary OS endpoint was not statistically significant for D+T or D vs SoC
- OS rate for D at 12 to 24 months was numerically higher than SoC

CI, confidence interval; ITT, intent-to-treat.

# EAGLE: OS by Treatment Arm and Response



## Number of patients at risk

### Responders

	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
D	43	43	43	43	41	41	40	38	34	30	24	24	21	16	9	5	2	0
D+T	45	45	45	42	41	38	35	32	25	22	17	16	14	6	5	2	0	0
SoC	43	43	42	37	32	27	22	17	12	8	5	4	3	2	1	0	0	0

### Nonresponders

	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
D	197	162	126	95	74	59	45	35	25	14	12	9	5	1	1	0	0	0
D+T	202	155	120	85	67	56	38	31	23	15	8	8	6	2	2	1	0	0
SoC	206	176	144	117	90	62	49	36	20	15	9	8	3	2	2	2	1	0

- OS was analyzed by responders (CR/PR) and nonresponders (SD/PD)
- Longer OS observed in responders for D and D+T, was not seen in nonresponders
  - Suggests responders with long OS cannot overcome the lack of OS improvement in nonresponders

# Webinar outline

- Development of the guideline
- Biomarkers
- Initiation, response monitoring and discontinuation of immunotherapy
- Immunotherapy sequencing
- Management of immune-related adverse events (*Dr. Licitra and Ms. Lewis*)
- Key takeaways

# Management of immune-related adverse events

## Expert Panel recommendations\*:

- *Monitoring is crucial to promptly identify and manage signs of progression, symptoms and adverse events. 53% of the Expert Panel recommends a one-month timeframe for initial clinical follow-up for identification of signs of immune-related symptoms and AEs.*
- *The majority of the Expert Panel (76%) recommends evaluating patients with HNSCC treated with checkpoint blockade for signs of adverse events at least once monthly during the course of treatment.*
- *The Expert Panel felt that general management of head and neck cancer toxicity is aligned with the practical management of irAEs in other solid tumor types. (SEE ICI-rAE CPG/Webinars)*

\*Guideline published July 15, 2019. Recommendations since updated.

# Management of immune-related adverse events

Expert Panel recommendations,\* continued:

- *Pneumonitis is not a greater concern in immunotherapy patients with HNSCC compared to other cancers. (67% Expert Panel agreement). However, some patients with HNSCC may be at a higher risk of developing pulmonary problems such as those already aspirating, or patients with previous radiation to the thorax.*
- *For irAE development  $\geq$  grade 3, the majority of the Expert Panel recommends admitting the patient to the hospital (79%), administering steroids (77%), and halting treatment (67%). The majority of the Expert Panel recommended routine monitoring of thyroid function (94%), neck and airway through imaging (62.5%), and AST/ALT levels (75%). Lipase evaluation was recommended by 44% of the Expert Panel, while brain imaging was only recommended by 6% of members. The Expert Panel was split on whether whole-body imaging is necessary during treatment. In patients that develop hypothyroidism, the majority of the Expert Panel (75%) recommended continuing immunotherapy, providing levothyroxine for management, and evaluating thyroid function in two-month intervals.*

*\*Guideline published July 15, 2019. Recommendations since updated.*

# Recognition and management of HNSCC-specific irAEs

- Bleeding from exposed neck vessels, including carotid artery rupture
- Airway compromise
- Facial edema
- Hypothyroidism

# Management of irAEs by grade

Grade 1: Difference in management for neurologic, hematologic, or cardiac toxicities

- *Most grade 1 toxicities , treatment can be continued with close monitoring.*
- *Important to note grade 1 anemia, lymphopenia, and thrombocytopenia patients can continue therapy with routine monitoring and infusion of blood products if needed.*
- **Any grade :** *Cardiac and neurologic toxicities are rare and occur in, 1% and < 6% of patients receiving IO regardless of solid tumor type, but can be severe and potentially fatal. Neuro toxicities increase to 12% in combination therapies.*
  - *Treatment of these specific AEs should be an MDC approach involving cardiologists and neurologists and patients are managed on a case by case basis.*

# Management of irAEs by grade

## Grade 1: Difference in management for neurologic, hematologic, or cardiac toxicities

- *Life threatening Myocarditis/pericarditis has been reported and mostly occurs within the first couple weeks of therapy. All grades warrant further work up, discontinuation of therapy and intervention to prevent cardiac compromise.*
- *Autoimmune neurologic toxicities including myasthenia gravis, GBS, Aseptic meningitis, encephalitis require prompt evaluation by neurologist, permanent discontinuation of IO. These irAEs can also correlate with myositis and cardiac toxicity*
- *Autoimmune hematologic toxicities include hemolytic anemia, acquired thrombotic thrombocytopenic purpura, aplastic anemia.*
- *TX includes high dose steroids methylpred pulse dosing 1g/day IV for 3-5 days versus 0.5mg/kg-2mg/kg dosing and switching to oral pred with taper over 4-6 weeks. If no response, consider other immunosuppressive agents and disease specific therapy per NCCN guidelines.*

# Management of irAEs by grade

## Grade 2: When to initiate steroids

- *The majority of the subcommittee recommends halting IO therapy short term and providing close monitored outpatient treatment.*
- *Low dose oral corticosteroids utilizing prednisone 1mg/kg are recommended for mild irAEs including rheumatologic, pneumonitis, colitis, hepatitis, AI, hypophysitis, and nephritis.*
- *Treatment can be resumed when the adverse reaction returns to grade 0-1 with prednisone or prednisone dose equivalent is 10mg or less.*

# Management of irAEs by grade

Grade 3: When to admit to the hospital and when to halt and discontinue treatment

- *The majority of the subcommittee recommends admitting patient to the hospital (79%) and administering steroids (77%) and halting treatment (67%).*
- *IV steroids 1mg-2mg/kg should be initiated with appropriate specialist consult. Further immunosuppressive therapies including infliximab, IVIG, Mycophenolate mofetil, Rituximab, Tocilizumab, ATG therapy for patients with severe irAEs that are steroid refractory after 48-72 hours. ICI should be permanently discontinued.*

# Monitoring for irAEs during treatment

- *Baseline PE, thorough patient history of autoimmune disease and organ specific disease should be taken prior to therapy.*
- *CBC with diff, CMP, cortisol should be completed prior to each treatment or every 4 weeks on treatment and every 6-12 weeks off therapy per NCCN guidelines.*
- *TSH every 4-6 weeks during therapy especially in head and neck cancer population.*
- *HgbA1c, amylase, lipase, Total T3, Free T 4, ACTH, CRP, CPK, ESR EKGs, PFTs, CTs as needed for evaluation for abnormal findings and symptoms.*

# Monitoring for long-term irAEs

- *Majority of clinical trials monitor for irAEs 90 to 100 days after the last immunotherapy infusion.*
- *Clinician should be aware of delayed irAEs that can occur months to years later after immunotherapy in any setting (neoadjuvant, definitive, adjuvant or recurrent metastatic setting)*
- *Most common chronic irAEs are mild: skin rash, hypothyroidism, and joint pain.*
- *Monitor patient indefinitely in survivorship care.*

# *Panel Discussion*

**Duration of therapy: Are all six cycles of chemotherapy needed?**



## Journal for ImmunoTherapy of Cancer

### Earn CME Credit as a *JITC* Reviewer

*JITC* also cooperates with reviewer recognition services (such as Publons) to confirm participation without compromising reviewer anonymity or journal peer review processes, giving reviewers the ability to safely share their involvement in the journal.

*Learn how to become a reviewer at  
[sitcancer.org/jitc](https://sitcancer.org/jitc)*



Society for Immunotherapy of Cancer

# Cancer Immunotherapy Clinical Practice Guidelines Mobile App

[sitcancer.org/CPG-app](https://sitcancer.org/CPG-app)

   #SITCGuidelines



# Thank you for attending the webinar!

Questions or comments: [connectED@sitcancer.org](mailto:connectED@sitcancer.org)