2020 ASCO®

ORL

Dr Daste (Oncologue médical, CHU Bordeaux

2020 ASCO

TPExtreme randomized trial: Quality of Life (QoL) and survival according to second-line treatments in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC)

Joël Guigay, Jérôme Fayette, Ricard Mesia Sr., Esma Saada-Bouzid, Cedrik Lafond, Lionnel Geoffrois, Laurent Martin, Olivier Capitain, Didier Cupissol, Helene Castanie, Alison Claire Johnson, Damien Vansteene, Caroline Even, Christian Sire, Raissa Kapso, Melissa Delhommeau, Cecile Chevassus-Clement, Ulrich Keilholz, Jean Bourhis, Anne Auperin, GORTEC - AIO Studien gGmbH - TTCC - Unicancer H&N

Centre Antoine Lacassagne, FHU OncoAge, Université Côte d'Azur, Nice, France; Centre Léon Bérard, Medical Oncology, Lyon, France; Catalan Institute of Oncology, IDIBELL, Barcelona, Spain; Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; Clinique Victor Hugo, Le Mans, France; Centre Alexis Vautrin, Vandoeuvre-Lès-Nancy, France; Radiotherapie, Centre G Le Conquerant, Le Havre, France; Institut de Cancerologie de l'Ouest, Site Paul Papin, Angers, France; Centre Val d'Aurelle, Montpellier, France; Hôpital Prive du Confluent S.A.S, Nantes, France; Centre François Baclesse, Caen, France; Institut de Cancerologie de l'Ouest–René Gauducheau, Nantes, France; Gustave Roussy, Villejuif, France; CH de Lorient, Lorient, France; Service de Biostatistique Et d'Épidémiologie, Gustave Roussy, Villejuif, France; GORTEC, Tours, France; Charité Comprehensive Cancer Center, Berlin, Germany; Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Sponsor: **GORTEC**

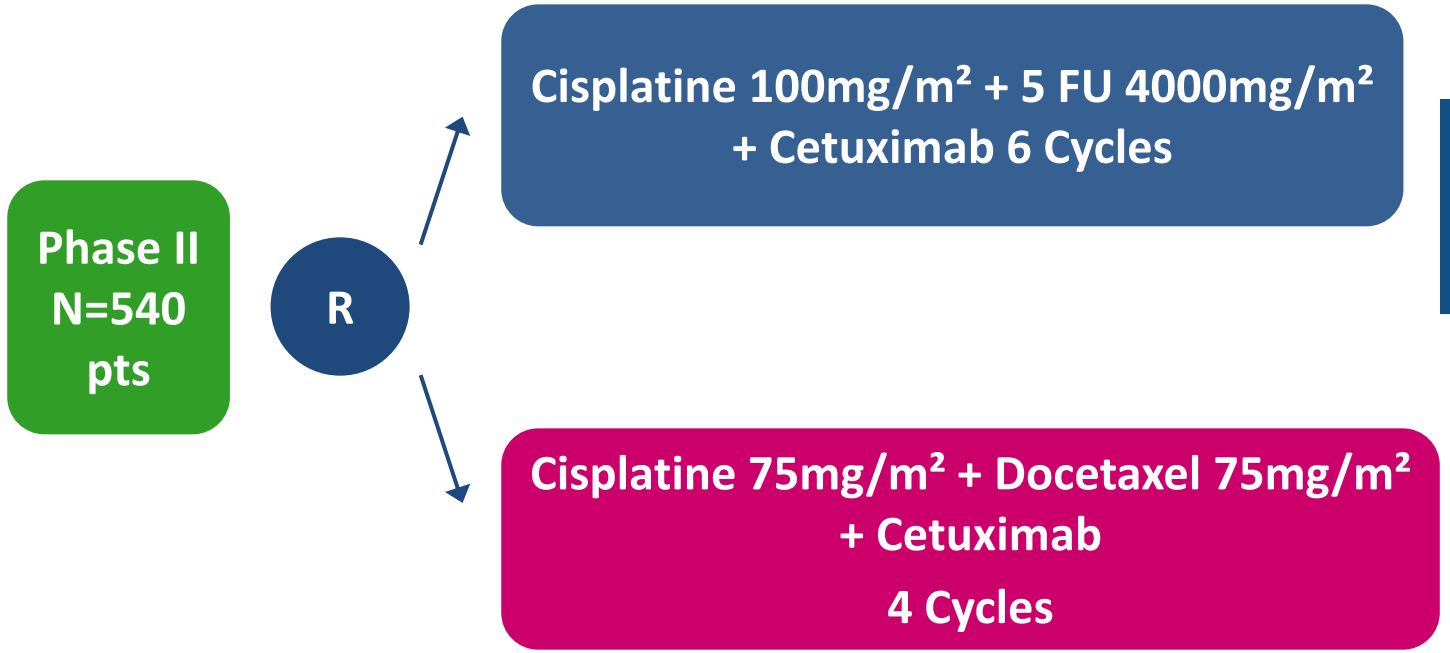
National Cooperative Groups coordination

FRANCE
Pr J. BOURHIS

SPAIN
Pr R. MESIA

GERMANY
Pr U. KEILHOLZ

TPEX Design



Median OS higher than expected:
14.5 months in TPEx arm and
13.4 months in EXTREME arm

HR=0.89 (95% CI: 0.74-1.08)
p-value=0.23

Objectif principal : OS

Objectif secondaire: ORR, BOR, PFS, time to progression, toxicity, compliance, QoL, net monetary benefit

Et après…2ème ligne

	EXTREME arm		TPEx arm	
Patients with 2nd line data available	256		245	
2nd line received	164 (64%)		157 (64%)	
Type of 2nd line				
IO (anti PD-1/PDL-1)	41 (16%)		41 (17%)	
Taxane based chemotherapy	56 (22%)	120 (47%)	30 (12%)	109 (44%)
Other chemotherapy	40 (16%)		61 (25%)	
Cetuximab +/- chemotherapy	24 (9%)		18 (7%)	
Radiotherapy	3 (1%)		7 (3%)	

- 79% and 85% of the 2nd line treatments were given after progression in EXTREME and TPEx arms, respectively.

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Survie de 2ème ligne

2nd line treatment: Overall Survival since start of 2nd line in each arm according to Chemo +/- Cetux vs IO

	EXTREME arm		TPEx arm	
	2nd line with chemo/cetux	2nd line with IO	2nd line with chemo/cetux	2nd line with IO
Overall survival at 12 months	39.4%	41.0%	25.1%	49.1%
Overall survival at 24 months	15.9%	9.8%	8.7%	27.8%
Overall survival at 36 months	7.3%	0%	5.8%	8.3%
Median OS (95%CI)	9.3 months (7.7 – 11.6)	8.3 months (5.0 – 15.0)	7.1 months (5.6 – 8.2)	11.6 months (6.0 – 21.4)

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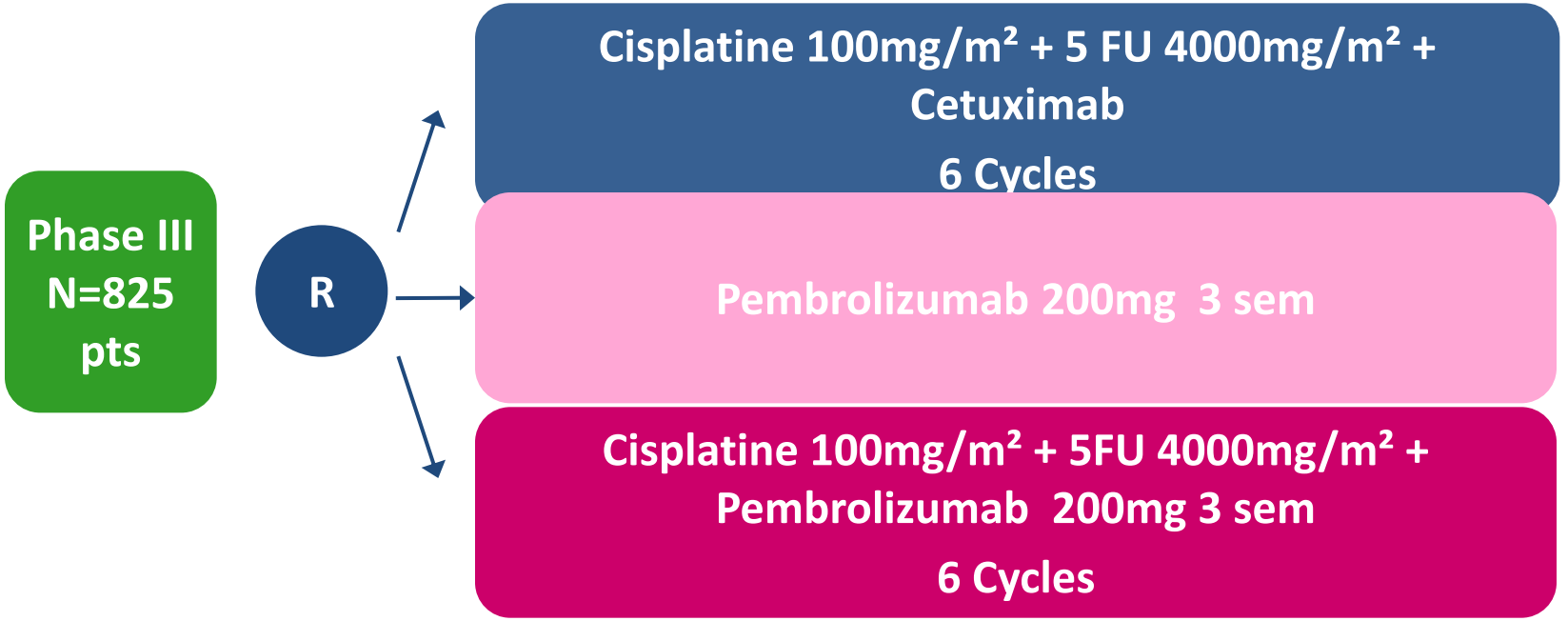
KEYNOTE-048: Progression After the Next Line of Therapy Following Pembrolizumab or Pembrolizumab Plus Chemotherapy vs EXTREME as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Kevin Harrington,[1] Danny Rischin,[2] Richard Greil,[3] Denis Soulieres,[4] Makoto Tahara,[5] Gilberto Castro,[6] Amanda Psyrri,[7] Neus Baste,[8] Prakash C. Neupane,[9] Åse Bratland,[10] Thorsten Fuereder,[11] Brett G. M. Hughes,[12] Ricard Mesia Sr.,[13] Nuttapong Ngamphaiboon,[14] Tamara Rordorf,[15] Wan Zamaniah Wan Ishak,[16] Yayan Zhang,[17] Burak Gumuscu,[17] Ramona F. Swaby,[17] Barbara Burtness[18]

[1]The Institute of Cancer Research/The Royal Marsden NHS Foundation Trust National Institute of Health Research Biomedical Research Centre, London, UK; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; [4]Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [7]National Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]University of Kansas Medical Center, Kansas City, KS, USA; [10]Oslo University Hospital, Oslo, Norway; [11]Medical University of Vienna, Vienna, Austria; [12]Royal Brisbane and Women's Hospital and University of Queensland, Brisbane, Australia; [13]Catalan Institute of Oncology, Hospitalet de Llobregat, Barcelona, Spain; [14]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [15]University Hospital, Zurich, Switzerland; [16]University of Malaya, Kuala Lumpur, Malaysia; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA

Keynote 048: Design



Augmentation de l'OS pour pembrolizumab seul ou en association selon le statut CPS

Objectif principal : OS PDL 1 expressing , PFS PDL 1 expressing, OS in all participants, PFS in all participants

Objectif secondaire: ORR, PFS at 6 months, PFS at 12 months, QoL

Et après

First Subsequent Therapy

n (%)	Pembro Monotherapy n = 301	Pembro + Chemotherapy n = 281	EXTREME n = 300
Any new anticancer treatment[a]	148 (49.2)	115 (40.9)	159 (53.0)
Chemotherapy	135 (44.9)	88 (31.3)	102 (34.0)
EGFR inhibitor	59 (19.6)	37 (13.2)	19 (6.3)
Immune checkpoint inhibitor	6 (2.0)	12 (4.3)	50 (16.7)
Other immunotherapy	1 (0.3)	0 (0.0)	6 (2.0)
Kinase inhibitor	1 (0.3)	7 (2.5)	1 (0.3)
Other	2 (0.7)	1 (0.4)	2 (0.7)

[a]A patient is counted only once for each therapy group, but a patient could be counted in more than one therapy group.
Data cutoff: February 25, 2019 (final analysis).

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Résultats PFS2

	CPS ≥ 20	CPS ≥ 1	Pop Total
Pembro	PFS 1 : 3.4 (3.2-3.8) PFS 2 : 11.7 (9.1-14.8)	PFS 1 : 3.2 (2.2-3.4) PFS 2 : 9.4 (8.3-10.2)	PFS 1 : 2.3 (2.3-3.3) PFS 2 : 9 (8.0-9.9)
Extrême	PFS 1 : 5 (4.8-6.2) PFS 2 : 9 .4 (7.9-10.8)	PFS 1 : 5 (4.8- 5.8) PFS 2 : 8.8 (8.3-9.8)	PFS 1 : 5.2 (4.9-6.0) PFS 2 : 9 (8.4-9.8)

Résultats PFS2

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Pembro +chimio	PFS 1 : 5.8 (4.7-7.6) PFS 2 : 11.3 (8.8-14.7)	PFS 1 : 5 (4.7-6.2) PFS 2: 10.3 (9.2-12.5)	PFS 1 : 4.9 (4.7-6.0) PFS2: 10.3 (9.3-11.9)
Extrême	PFS1 : 5.2 (4.8- 6.2) PFS 2 : 9 .7 (8.4-11.0)	PFS1 : 5 (4.8-5.8) PFS2 : 8.9 (8.4-9.8)	PFS1 : 5.1 (4.9-6.0) PFS2 : 9 (8.6-10.0)

JCOG
Japan Clinical Oncology Group

Phase II/III Trial of Post-operative Chemoradiotherapy Comparing 3-Weekly Cisplatin with Weekly Cisplatin in High-risk Patients with Squamous Cell Carcinoma of the Head and Neck（JCOG1008）

Naomi Kiyota, Makoto Tahara, Hirofumi Fujii, Tomoko Yamazaki, Hiroki Mitani, Shigemichi Iwae, Yasushi Fujimoto, Yusuke Onozawa, Nobuhiro Hanai, Takenori Ogawa, Hiroki Hara, Nobuya Monden, Eiji Shimura, Shujiro Minami, Takashi Fujii, Kaoru Tanaka, Takeshi Kodaira, Junki Mizusawa, Kenichi Nakamura, Ryuichi Hayashi

Head and Neck Cancer Study Group of the Japan Clinical Oncology Group (JCOG-HNCSG)

Japan Registry of Clinical Trials Registry Number: jRCTs031180135

PRESENTED BY: Naomi Kiyota, MD, PhD, Kobe University Hospital, Japan, E-mail: nkiyota@med.kobe-u.ac.jp

Design

28 Centres-max 56j de la chirurgie

Post-op haut risque:
- stade III-IV
- Marges microscopiquement envahies et/ou rupture capsulaire (RC)

Stratification:
- Marges microscopiquement envahies et/ou rupture capsulaire (RC)
- Centre

N=261
Oct 12-
Dec 18

R

RTT (66Gy-33fr) + Cisplatine 100mg/m², Q3W

RTT (66Gy-33fr) + Cisplatine 40mg/m², W

Objectif principal : OS

Population

Characteristic		Arm A: 3-Weekly CDDP+RT (N=132)	Arm B: Weekly CDDP+RT (N=129)
Age	Median (range)	62 (26-75)	61 (20-75)
Sex	Female	22	19
	Male	110	110
ECOG-PS	0	92	94
	1	40	35
Primary site	Oral cavity	61	60
	Larynx	12	11
	Oropharynx	14	21
	Hypopharynx	45	37

Characteristic		Arm A: 3-Weekly CDDP+RT (N=132)	Arm B: Weekly CDDP+RT (N=129)
High-risk factors*	Positive margin	43	42
	Extra-nodal extension	112	109
Pathological T	T1	13	7
	T2	26	40
	T3	25	23
	T4	68	59
Pathological N	N0	9	6
	N1	10	15
	N2	107	104
	N3	5	2
	Nx	1	2

*overlapped

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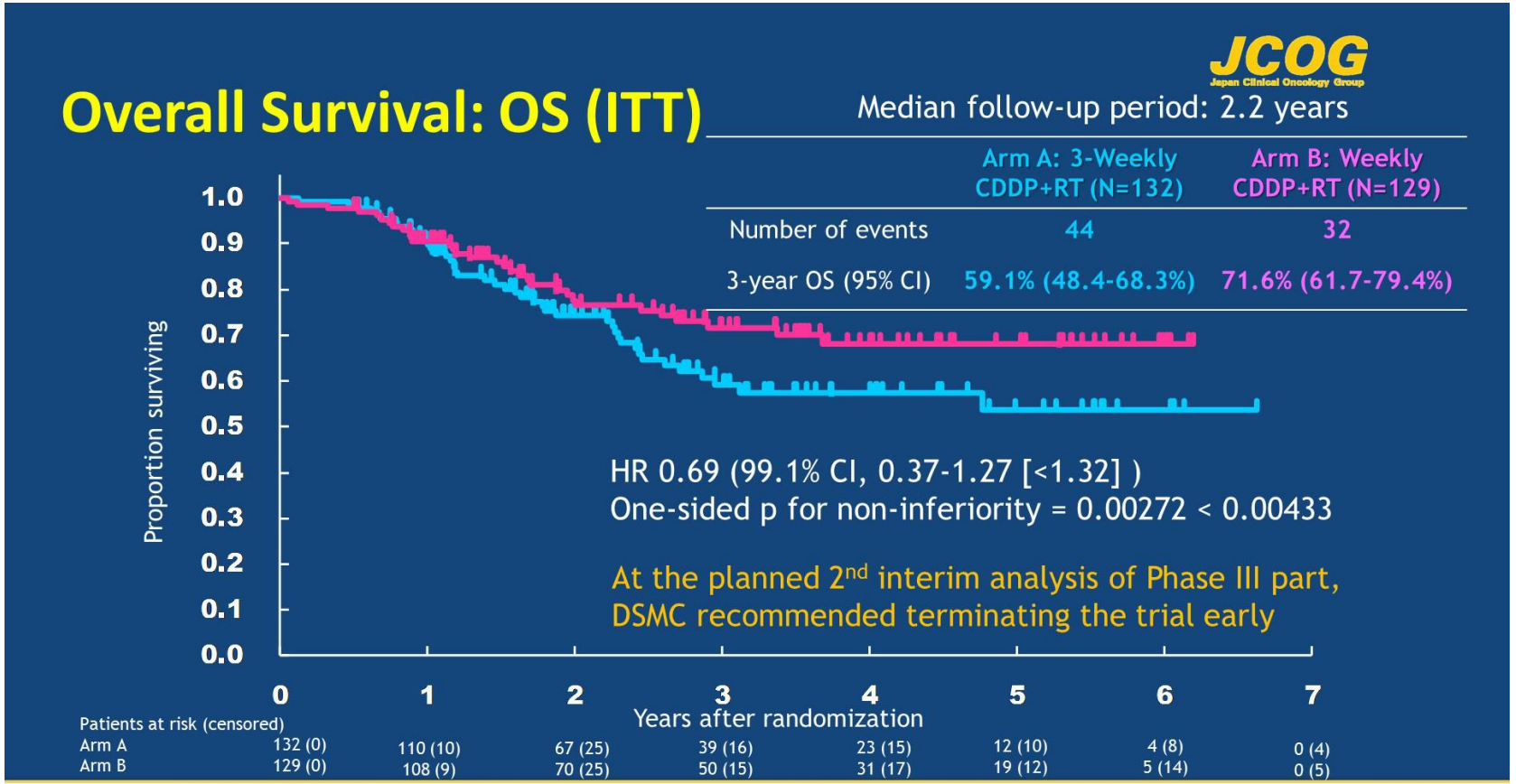
Résultat: OS


JCOG
Japan Clinical Oncology Group
Overall Survival: OS (ITT)
Median follow-up period: 2.2 years
Arm A: 3-Weekly CDDP+RT (N=132)
Arm B: Weekly CDDP+RT (N=129)
Number of events 44 32
3-year OS (95% CI) 59.1% (48.4-68.3%) 71.6% (61.7-79.4%)
Proportion surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
HR 0.69 (99.1% CI, 0.37-1.27 [<1.32])
One-sided p for non-inferiority = 0.00272 < 0.00433
At the planned 2nd interim analysis of Phase III part, DSMC recommended terminating the trial early
0 1 2 3 4 5 6 7
Years after randomization
Patients at risk (censored)
Arm A 132 (0) 110 (10) 67 (25) 39 (16) 23 (15) 12 (10) 4 (8) 0 (4)
Arm B 129 (0) 108 (9) 70 (25) 50 (15) 31 (17) 19 (12) 5 (14) 0 (5)

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Profil de tolérance en faveur du bras weekly

Hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade 3-4 (%)	Any grade	Grade 3-4
Total	129 (100%)	79 (61.2%)	122 (100%)	79 (64.8%)
Leukopenia	123 (95.3%)	71 (55.0%)	114 (93.4%)	75 (61.5%)
Neutropenia	118 (91.5%)	63 (48.8%)	106 (86.9%)	43 (35.3%)
Anemia	129 (100%)	18 (14.0%)	122 (100%)	16 (13.1%)
Thrombocytopenia	85 (65.9%)	3 (2.3%)	102 (83.6%)	4 (3.3%)
Febrile neutropenia	7 (5.4%)	7 (5.4%)	5 (4.1%)	5 (4.1%)

Non-hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade3-4(%)	Any grade	Grade3-4
Mucositis	118 (91.5%)	30 (23.3%)	113 (92.6%)	34 (27.9%)
Dysphagia	75 (58.1%)	24 (18.6%)	59 (48.4%)	14 (11.5%)
Dermatitis	118 (91.4%)	19 (14.7%)	112 (91.8%)	14 (11.5%)
Nausea	87 (67.4%)	17 (13.2%)	57 (46.7%)	6 (4.9%)
Infection	25 (19.4%)	15 (11.6%)	18 (14.8%)	8 (6.6%)
Hyponatremia	119 (92.2%)	13 (10.1%)	100 (82.0%)	13 (10.7%)
Renal impairment	51 (39.5%)	0 (0%)	36 (29.5%)	0 (0.0%)
Hearing impairment	22 (17.1%)	5 (3.9%)	9 (7.4%)	2 (1.6%)
Peripheral neuropathy	7 (5.4%)	0 (0.0%)	2 (1.6%)	0 (0.0%)

- *Grade 3 or more toxicities which occurred in ≥10% patients or toxicities of special interest

A retenir

- TPEX
  - Séquence ? Taxane suivi d'IO
- Keynote 048
  - IO marche même après
- Radiothérapie potentialisée
  - En adjuvant, cisplatine 40mg/m²/semaine est une option

En vrac

- Ganglion sentinelle pour T1/T2 N0 cavité buccale oropharynx
- Dé-escalade de radiothérapie
  - Epargne muscle masticateur
  - Diminution dose pour oropharynx pronostic intermédiaire
- Nouvelle combinaison d'IO
- Médecine personnalisée: anti HRAS
- CAK: axitinib
- Nasopharynx chimiothérapie néo-adj ou adj
- IO: Attention au ATB et TMB??

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Des questions ?

Merci de votre écoute