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LBA36

Nivolumab (N) + ipilimumab (I) vs EXTREME as first-line (1L) treatment (tx) for recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN): Final results of CheckMate 651

A. Argiris[1,21], K. Harrington[2], M. Tahara[3], R.L. Ferris[4], M. Gillison[5], J. Fayette[6], A. Daste[7], P. Koralewski[8], R. Mesia Nin[9], N.F. Saba[10], M. Mak[11], M.A. Álvarez Avitia[12], A. Guminski[13], U. Müller-Richter[14], N. Kiyota[15], M. Roberts[16], T.A. Khan[17], K. Miller-Moslin[18], L. Wei[19], R. Robert Haddad[20]

[1] Medical Oncology, Hygeia Hospital, Marousi, Greece, [21] Thomas Jefferson University, Philadelphia, PA, USA, [2] Division of Radiotherapy and Imaging, Royal Marsden Hospital/The Institute of Cancer Research, London, UK, [3] Department of Head and Neck Medical Oncology, National Cancer Center Hospital East, Kashiwa, Chiba, Japan, [4] Departments of Otolaryngology, Immunology and Radiation Oncology, UPMC Hillman Cancer Center, Pittsburgh, PA, USA, [5] Department of Thoracic-Head & Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [6] Department of Clinical Oncology, Centre Léon Bérard, Lyon, France, [7] Oncologie Medicale, Hôpital Saint-André, Bordeaux, France, [8] Medical Oncology, Wojewodzki Szpital Specjalistyczny im. Ludwika Rydygiera w Krakowie, Krakow, Poland, [9] Medical Oncology, Catalan Institut of Oncology, L'Hospitalet de Llobregat, Barcelona, Spain, [10] Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA, [11] Medical Oncology, Instituto do Câncer do Estado de São Paulo, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, [12] Medical Oncology, Instituto Nacional De Cancerología, Mexico City, Mexico, [13] Oncology Care North, Royal North Shore Hospital, Sydney, NSW, Australia, [14] Department of Oral and Maxillofacial Plastic Surgery, University Hospital Würzburg, Bavarian Cancer Research Center (BZKF), Würzburg, Germany, [15] Cancer Center, Kobe University Hospital, Kobe, Japan, [16] Oncology Translational Medicine, Bristol Myers Squibb, Princeton, NJ, USA, [17] Oncology Clinical Development, Bristol Myers Squibb, Princeton, NJ, USA, [18] Oncology Clinical Science, Bristol Myers Squibb, Princeton, NJ, USA, [19] Biostatistics, Bristol Myers Squibb, Princeton, NJ, USA[20] Division of Head and Neck Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Background

Despite recent tx advances in R/M SCCHN, durable survival benefit remains an elusive goal. CheckMate 651 (NCT02741570), a phase 3 randomized trial, evaluated N+I vs EXTREME regimen as 1L tx for platinum-eligible R/M SCCHN.

Methods

Pts with R/M SCCHN, no prior systemic therapy in R/M setting, and ECOG PS 0–1 were randomized 1:1 to N (3 mg/kg Q2W) + I (1 mg/kg Q6W; n = 472), or EXTREME (n = 475), stratified by tumor PD-L1 level, p16 expression, and prior chemotherapy. Pts were treated with N+I or EXTREME (cetuximab + cisplatin/carboplatin + fluorouracil ≤6 cycles, then cetuximab maintenance) until progression/unacceptable toxicity, or 2 y for N+I. Primary endpoints were overall survival (OS) in all randomized and PD-L1 combined positive score (CPS) ≥20 populations. OS in CPS ≥1 was a key secondary endpoint. Progression-free survival (PFS), objective response rate (ORR), duration of response (DOR), and safety were also assessed.

Results

947 pts were randomized; baseline characteristics were balanced across arms. At final analysis (minimum follow-up: 27.3 mo), there was no statistically significant improvement in OS with N+I vs EXTREME in all randomized (HR 0.95 [97.9% CI: 0.80–1.13] $P = 0.4951$) or CPS ≥20 (HR 0.78 [97.5% CI: 0.59–1.03] $P = 0.0469$) populations. In pts with CPS ≥1, OS HR was 0.82 (95% CI: 0.69–0.97). Other efficacy results are in the table. Overall, 8% (N+I) and 46% (EXTREME) of pts received subsequent immunotherapy. Grade 3/4 tx-related adverse events occurred in 28% vs 71% of treated pts, respectively.

Conclusions

N+I did not show statistically significant OS improvement vs EXTREME in pts with R/M SCCHN; however, there was evidence of clinical activity in pts with CPS ≥20 and CPS ≥1 as shown by prolonged OS (median and 2 y rates) and durable responses. Notably, OS in the control arm was better than historical data. N+I had a favorable safety profile vs EXTREME, with no new safety signals observed.Table: LBA36

	All randomized		CPS ≥20		CPS ≥1	
	N+I	EXTREME	N+I	EXTREME	N+I	EXTREME
n	472	475	185	178	355	372

	All randomized		CPS ≥20		CPS ≥1	
	N+I	EXTREME	N+I	EXTREME	N+I	EXTREME
Median OS, mo 95% CI	13.9 12.1–15.8	13.5 12.6–15.2	17.6 13.8–22.0	14.6 12.3–16.0	15.7 13.7–18.8	13.2 11.1–14.6
HR CI	0.95 97.9% CI: 0.80–1.13	0.78 97.5% CI: 0.59–1.03	0.82 95% CI: 0.69–0.97			
P value	0.4951	0.0469	-			
2-y OS, %	31	28	41	33	34	28
Median PFS, mo95% CI	3.32.8–4.2	6.75.8–7.0	5.43.1–6.9	7.05.6–8.7	4.2 2.9-5.4	6.1 5.6-7.0
HR 95% CI	1.41 1.21–1.65	1.02 0.78–1.33	1.23 1.03–1.47			
2-y PFS, %	15	13	26	16	18	13
ORR, n (%) 95% CI	114 (24) 20–28	175 (37) 32–41	63 (34) 27–41	64 (36) 29–44	98 (28) 23-33	133 (36) 31-41
Median DOR, mo 95% CI	16.69.7–29.4	5.95.5–7.0	32.612.1–NR	7.05.7–10.1	18.3 10.9-32.6	6.0 5.6-7.6
18 mo DOR, %	48	20	62	29	52	22

Clinical trial identification

NCT02741570.

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A. Argiris: Financial Interests, Personal, Other, Review Committee: AstraZeneca; Financial Interests, Personal, Funding: BMS; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Other, Review Committee: Debiopharm; Financial Interests, Personal, Invited Speaker: Merck Serono; Financial Interests, Personal, Advisory Board: Rakuten Medical, Inc.; Financial Interests, Personal, Funding: Rakuten Medical, Inc. K. Harrington: Financial Interests, Institutional, Advisory Board: Arch Oncology; Financial Interests, Institutional, Advisory Board: AstraZeneca; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Advisory Board: BMS; Financial Interests, Institutional, Invited Speaker: BMS; Financial Interests, Institutional, Advisory Board: Boehringer-Ingelheim; Financial Interests, Institutional, Research Grant: Boehringer-Ingelheim; Financial Interests, Institutional, Advisory Board: Codiak; Financial Interests, Institutional, Advisory Board: Inzen; Financial Interests, Institutional, Advisory Board: Merck-Serono; Financial Interests, Institutional, Invited Speaker: Merck-Serono; Financial Interests, Personal and Institutional, Advisory Board: MSD; Financial Interests, Personal and Institutional, Invited Speaker: MSD; Financial Interests, Personal and Institutional, Research Grant: MSD; Financial Interests, Institutional, Advisory Board: Oncolys; Financial Interests, Institutional, Advisory Board: Pfizer; Financial Interests, Institutional, Advisory Board: PsiVac; Financial Interests, Institutional, Advisory Board: Replimune; Financial Interests, Institutional, Research Grant: Replimune. M. Tahara: Financial Interests, Personal and Institutional, Invited Speaker: Ono Pharmaceutical; Financial Interests, Personal and Institutional, Advisory Board: Ono Pharmaceutical; Financial Interests, Personal and Institutional, Research Grant: Ono Pharmaceutical; Financial Interests, Personal and Institutional, Invited Speaker: BMS; Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Research Grant: BMS; Financial Interests, Personal and Institutional, Invited Speaker: MSD; Financial Interests, Personal and Institutional, Advisory Board: MSD; Financial Interests, Personal and Institutional, Research Grant: MSD; Financial Interests, Personal and Institutional, Invited Speaker: Bayer; Financial Interests, Personal and Institutional, Advisory Board: Bayer; Financial Interests, Personal and Institutional, Research Grant: Bayer; Financial Interests, Personal and Institutional, Invited Speaker: Merck Biopharma; Financial Interests, Personal and Institutional, Advisory Board: Merck Biopharma; Financial Interests, Personal and Institutional, Research Grant: Merck Biopharma; Financial Interests, Personal and Institutional, Invited Speaker: Eisai; Financial Interests, Personal and Institutional, Advisory Board: Eisai; Financial Interests, Personal and Institutional, Research Grant: Eisai; Financial Interests, Personal, Advisory Board: LOXO; Financial Interests, Personal, Advisory Board: Celgene; Financial Interests, Personal and Institutional, Invited Speaker: Rakuten Medical; Financial Interests, Personal and Institutional, Advisory Board: Rakuten Medical; Financial Interests, Personal and Institutional,

Research Grant: Rakuten Medical; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal and Institutional, Advisory Board: Novartis; Financial Interests, Personal and Institutional, Research Grant: Novartis. R.L. Ferris: Financial Interests, Personal, Advisory Board: Achilles Therapeutics; Financial Interests, Personal, Advisory Role: Aduro Biotech, Inc; Financial Interests, Institutional, Funding: AstraZeneca/MedImmune; Financial Interests, Personal, Advisory Role: Bicara Therapeutics, Inc; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Institutional, Funding: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: EMD Serono; Financial Interests, Personal, Advisory Role: Everest Clinical Research Corporation; Financial Interests, Personal, Advisory Role: F. 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Gillison: Financial Interests, Personal and Institutional, Advisory Role: Istari Oncology Inc; Financial Interests, Personal and Institutional, Advisory Role: LLX Solutions, LLC; Financial Interests, Personal and Institutional, Advisory Role: Kura Oncology; Financial Interests, Personal and Institutional, Advisory Role: Mirati Therapeutics; Financial Interests, Personal and Institutional, Advisory Role: BioNtech AG; Financial Interests, Personal and Institutional, Advisory Role: Shattuck Labs, Inc; Financial Interests, Personal and Institutional, Advisory Role: EMD Serono, Inc; Financial Interests, Personal and Institutional, Advisory Role: Depiopharm; Financial Interests, Personal and Institutional, Advisory Role: Merck & Co; Financial Interests, Personal and Institutional, Advisory Role: Ipsen Biopharmaceuticals Inc; Financial Interests, Personal and Institutional, Advisory Role: Gilead Sciences, Inc; Financial Interests, Personal and Institutional, Advisory Role: Bristol Myers Squibb; Financial Interests, Personal and Institutional, Advisory Role: Bicara Therapeutics; Financial Interests, Personal and Institutional, Advisory Role: Bayer Healthcare Pharmaceutics; Financial Interests, Personal and Institutional, Advisory Role: Genocea Biosciences, Inc.; Financial Interests, Personal and Institutional, Invited Speaker: OncLive; Financial Interests, Personal and Institutional, Invited Speaker: Roche; Financial Interests, Personal and Institutional, Advisory Role, Scientific advisory committee: Seagen; Financial Interests, Personal and Institutional, Advisory Role, Scientific advisory committee: Sensei Biotherapeutics, Inc; Financial Interests, Personal and Institutional, Funding, Research funding: Genocea Biosciences, Inc; Financial Interests, Personal and Institutional, Invited Speaker, Research funding: Bristol Myers Squibb; Financial Interests, Personal and Institutional, Invited Speaker, Research funding: Genentech; Financial Interests, Personal and Institutional, Invited Speaker, Research funding: Kura; Financial Interests, Personal and Institutional, Invited Speaker, Research funding: Cullinan Labs; Financial Interests, Personal and Institutional, Other, DSBM: SQZBiotech; Financial Interests, Personal and Institutional, Other, DSBM: BioMimetix. J. Fayette: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: Innate Pharma,; Financial Interests, Personal, Advisory Board: Merck Serono,; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Institutional, Other, Research Funding: Seagens; Non-Financial Interests, Personal, Principal Investigator: AstraZeneca . A. Daste: Financial Interests, Personal, Advisory Role, Consulting: Bristol Myers Squibb; Financial Interests, Personal, Advisory Role, Consulting: Merck, Sharp & Dohme; Financial Interests, Personal, Advisory Role, Consulting: Merck. R. Mesia Nin: Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Personal, Invited Speaker: Merck, Sharp & Dohme; Financial Interests, Personal, Invited Speaker: Merck; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Merck, Sharp & Dohme; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Nanobiotics; Financial Interests, Personal, Advisory Board: Seattle Genetics; Financial Interests, Personal, Advisory Board: Boeringer Ingelheim. N.F. Saba: Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: Kura; Financial Interests, Personal, Advisory Board: CUE; Financial Interests, Institutional, Funding: Bristol Myers Squibb; Financial Interests, Institutional, Funding: Exelixis; Financial Interests, Personal, Advisory Role: Pfizer . M. Mak: Financial Interests, Personal, Invited Speaker: Bayer; Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Invited Speaker: Merck Serono; Financial Interests, Personal, Invited Speaker: Takeda; Financial Interests, Personal, Invited Speaker: Amgen. M.A. Álvarez Avitia: Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Invited Speaker: Janssen Mexico; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Invited Speaker: Merck, Sharp & Dohme; Financial Interests, Personal, Advisory Board: Merck, Sharp & Dohme; Financial Interests, Personal, Invited Speaker: Ipsen. A. Guminski: Financial Interests, Personal, Advisory Board: BMS; Non-Financial Interests, Personal, Other, Conference Travel Support: BMS; Financial Interests, Personal, Advisory Board: Regeneron; Non-Financial Interests, Personal, Principal Investigator: Regeneron; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Merck KgA; Non-Financial Interests, Personal, Other, Conference Travel Support: Merck KgA; Non-Financial Interests, Personal and Institutional, Principal Investigator, Investigator Initiated Trial Support: AstraZeneca; Financial Interests, Personal, Advisory Board: MSD; Non-Financial Interests, Personal and Institutional, Research Grant: Sun Pharma; Financial Interests, Personal, Advisory Board: Sun Pharma. U. Müller-Richter: Non-Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Non-Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Non-

Financial Interests, Institutional, Funding: Bristol Myers Squibb; Non-Financial Interests, Institutional, Principal Investigator: Bristol Myers Squibb; Non-Financial Interests, Personal, Invited Speaker: Merck, Sharp & Dohme; Non-Financial Interests, Personal, Advisory Board: Merck, Sharp & Dohme; Non-Financial Interests, Personal, Invited Speaker: Merck, Sharp & Dohme; Non-Financial Interests, Personal, Expert Testimony: Merck, Sharp & Dohme; Non-Financial Interests, Institutional, Funding: Merck, Sharp & Dohme; Financial Interests, Institutional, Principal Investigator: Merck, Sharp & Dohme; Non-Financial Interests, Personal, Advisory Board: Sanofi; Non-Financial Interests, Personal, Expert Testimony: Sanofi; Non-Financial Interests, Personal, Writing Engagements: Sanofi; Non-Financial Interests, Institutional, Funding: KuraOncology; Non-Financial Interests, Institutional, Principal Investigator: KuraOncology; Non-Financial Interests, Institutional, Funding: AstraZeneca; Non-Financial Interests, Institutional, Principal Investigator: AstraZeneca; Non-Financial Interests, Institutional, Funding: BioNTech; Non-Financial Interests, Institutional, Principal Investigator: BioNTech. N. Kiyota: Financial Interests, Personal, Speaker's Bureau, Speaker of sponsored seminar: Bayer; Financial Interests, Personal, Speaker's Bureau, Speaker of sponsored seminar: Eisai; Financial Interests, Personal, Speaker's Bureau, Speaker of sponsored seminar: ONO; Financial Interests, Personal, Speaker's Bureau, Speaker of sponsored seminar: Bristol Myers Squibb; Financial Interests, Personal, Speaker's Bureau, Speaker of sponsored seminar: Merck, Sharp & Dohme; Financial Interests, Institutional, Research Grant: Adlai Nortye; Financial Interests, Institutional, Research Grant: Bayer; Financial Interests, Institutional, Research Grant: ONO; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Lilly; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb; Financial Interests, Institutional, Research Grant: Rakuten Medical; Financial Interests, Institutional, Advisory Role: Adlai Nortye; Financial Interests, Institutional, Advisory Role: ONO. M. Roberts: Financial Interests, Personal, Full or part-time Employment: BMS; Financial Interests, Personal, Stocks/Shares: BMS . T.A. Khan: Financial Interests, Personal, Full or part-time Employment: BMS; Financial Interests, Personal, Stocks/Shares: BMS. K. Miller-Moslin: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb. L. Wei: Financial Interests, Personal, Full or part-time Employment: BMS. R. Robert Haddad: Financial Interests, Personal, Full or part-time Employment: Dana-Farber Cancer Institute; Financial Interests, Personal, Leadership Role: National Comprehensive Cancer Network; Financial Interests, Personal, Advisory Role: Celgene; Financial Interests, Personal, Advisory Role: Merck; Financial Interests, Personal, Advisory Role: Eisai; Financial Interests, Personal, Advisory Role: Bristol Myers Squibb; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Loxo; Financial Interests, Personal, Advisory Role: Genentech; Financial Interests, Personal, Advisory Role: Immunomic Therapeutics; Financial Interests, Personal, Advisory Role: GSK; Financial Interests, Personal, Advisory Role: Gilead Sciences; Financial Interests, Personal, Advisory Role: Vaccinex; Financial Interests, Personal, Advisory Role: EMD Serono; Financial Interests, Personal, Advisory Role: BioNTech AG; Financial Interests, Personal, Advisory Role: Achilles Therapeutics; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Mirati Therapeutics; Financial Interests, Institutional, Funding, Research Funding: Boehringer Ingelheim; Financial Interests, Institutional, Funding, Research Funding: Merck; Financial Interests, Institutional, Funding, Research funding: Bristol Myers Squibb; Financial Interests, Institutional, Funding, Research funding: Celgene; Financial Interests, Institutional, Funding, Research funding: AstraZeneca; Financial Interests, Institutional, Funding, Research Funding: VentiRx; Financial Interests, Institutional, Funding, Research Funding: Genentech; Financial Interests, Institutional, Funding, Research Funding: Pfizer; Financial Interests, Institutional, Funding, Research Funding: Kura; Financial Interests, Personal, Other: Nanobiotix; Financial Interests, Personal, Other: ISA Pharmaceuticals; Financial Interests, Personal, Other, Patents, Royalties, Other Intellectual Property: UpToDate. All other authors have declared no conflicts of interest.