9-1-2022

655MO Quality of life in patients with p16+ oropharyngeal cancer receiving accelerated radiotherapy (RT) with either cisplatin or cetuximab in NRG/RTOG 1016

J. Ringash

L. DeMora

M. L. Gillison

D. J. Adelstein

P. Harari

See next page for additional authors

Authors

J. Ringash, L. DeMora, M. L. Gillison, D. J. Adelstein, P. Harari, E. M. Sturgis, E. M. Basch, S. A. Koyfman, G. A. Krempl, D. M. Blakaj, J. E. Bates, T. Galloway, C. U. Jones, B. M. Beadle, P Torres-Saavedra, Q. T. Le, and Benjamin Movsas

not confirmed later. At baseline, HPV16ctDNA was positive in 34 of 47 tested pts. Among them, DNA ranged from 33 to 38275 cp/mL and 21 pts were tested after CRT and all had complete clearance.

Conclusions: N prior to CRT did not reach the expected feasibility aim, due to decreased Cis dose (renal/ototoxicity), potentially related to N. Progression-free and overall survival will be evaluated in both arms.

Clinical trial identification: NCT03838263.

Legal entity responsible for the study: Unicancer.

Funding: Partial funding from BMS - study CA209-970.

Disclosure: H. Mirghani: Financial Interests, Institutional, Advisory Role: MSD; Financial Interests, Institutional, Other, Travel, acommodation exepenses: BMS. C. Even: Financial Interests, Personal, Advisory Board: BMS, MSD, Innate Pharma, Merck Serono; Financial Interests, Institutional, Advisory Board: F Star Therapeutics; Financial Interests, Institutional, Invited Speaker: BMS, AstraZeneca, ISA pharmaceutics, MSD, DebioPharma, Ayala, Novartis. H. Pere: Financial Interests, Institutional, Invited Speaker: MSD, Janssen; Financial Interests, Institutional, Advisory Role: Seegen. J. Fayette: Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, MSD, Innate Pharma, Merck Serono, Roche; Financial Interests, Institutional, Other, research funding: Seagen; Non-Financial Interests, Principal Investigator: AstraZeneca. L. Geoffrois: Financial Interests, Personal, Advisory Board, Ad Board RCC: Ipsen; Financial Interests, Personal, Invited Speaker: Ipsen, BMS, Merck Serono, MSD; Financial Interests, Personal, Advisory Board, Ad Board Bladder Cancer: Merck Serono; Financial Interests, Personal, Advisory Board, Melanoma: Novartis; Financial Interests, Personal, Advisory Board, Head and Neck/RCC: MSD; Financial Interests, Personal, Advisory Board, Bladder cancer: Pfizer; Financial Interests, Institutional, Invited Speaker: MSD, BMS, Roche; Financial Interests, Institutional, Research Grant: Novartis. F. Clatot: Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Personal, Advisory Role: Merck Serono, MSD, BMS, Roche, Lilly, AstraZeneca. Y. Tao: Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Other, travel: MSD, Merck Serono. C. Badoual: Financial Interests, Personal, Invited Speaker: Merck. A. Auperin: Financial Interests, Personal, Funding: F. Hoffmann-La Roche. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.777

654MO High dimensional immuno-phenotyping of immunotherapy response in head and neck cancer

K.J. O'Byrne[1], N. Ma[2], H. Sadeghirad[3], N. Jhaveri[2], J. Monkman[3], A. Pratapa[2], B. Ben Cheikh[2], R. Ladwa[4], B.G.M. Hughes[5], O. Braubach[2], A. Kulasinghe[6]

[1]Cancer Services, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia; [2]Akoya Biosciences, Akoya Biosciences - East Coast, Hopkinton, CA, USA; [3]Diamantina Institute, The University of Queensland, St Lucia, QLD, Australia; [4]Medical Oncology Department, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia; [5]Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, QLD, Australia; [6]Diamantina Institute, University of Queensland, Brisbane, QLD, Australia

Background: Immunotherapies, in particular immune check point inhibitors (ICI), have proven to be game changing treatments of mucosal head and neck squamous cell cancer (HNSCC). Emerging successes with anti-PD-1/PD-L1 ICI therapy have lead to durable responses and prolonged survival in human papillomavirus positive (HPV+) and negative (HPV-) patients, and there is now an urgent need for predictive biomarkers to guide patient selection for highly targeted ICI therapies. There are currently no means by which to determine whether a patient would respond to anti PD-1/PD-L1 immunotherapy. Studies in the tumour microenvironment (TME) have demonstrated that a high degree of T-cell infiltration provides fertile grounds for effective ICI.

Methods: In this project, we used high dimensional spatial biomarker profiling to characterise the TME using targeted (region of interest) and unbiased (whole slide imaging) of metastatic/recurrent HNSCC tumours from a cohort of patients (n=40) treated with Pembrolizumab/Nivolumab. The discovery cohort consisted of patients who had complete/partial/stable/progressive response to ICI therapy. We first analysed tissues using targeted panel, GeoMx digital spatial profiling (Nanostring Technologies) of 80 protein targets simultaneously across immune cell profiles, immune-modulatory targets and IO-drug targets. We then expanded this to ultra-high plex antibody imaging with the Phenocylcer Fusion platform (Akoya Biosciences) of over 50 antibodies to derive single cell phenotypic signatures that could offer cues as to which treatment matches best with certain outcome groups.

Results: Our study identified stromal tissue signatures, specifically, VISTA, CD44, CD127 associated with resistance to immunotherapy. Most notably, high expression of VISTA within the stromal compartment was associated with a worse overall survival (p=0.0062). Using whole slide tissue imaging of single cell proteomic readouts, we were able to co-localise this signature to cell types within the tumour microenvironment.

Conclusions: Our study demonstrates the complementarity of targeted proteomic discovery and whole tissue imaging to identify biomarkers associated with response to ICI therapy in HNSCC.

Legal entity responsible for the study: The University of Queensland.

Funding: The Passe and Williams Foundation.

Disclosure: N. Ma, N. Jhaveri, A. Pratapa: Other, Institutional, Full or part-time Employment: Akoya Biosciences; Financial Interests, Institutional, Stocks/Shares: Akoya Biosciences. B. Ben Cheikh, O. Braubach: Non-Financial Interests, Institutional, Full or part-time Employment: Akoya Biosciences; Financial Interests, Institutional, Stocks/Shares: Akoya Biosciences. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.778

655MO Quality of life in patients with p16+ oropharyngeal cancer receiving accelerated radiotherapy (RT) with either cisplatin or cetuximab in NRG/RTOG 1016

J. Ringash[1], L. DeMora[2], M.L. Gillison[3], D.J. Adelstein[4], P. Harari[5], E.M. Sturgis[6], E.M. Basch[7], S.A. Koyfman[8], G.A. Krempl[9], D.M. Blakaj[10], J.E. Bates[11], T. Galloway[12], C.U. Jones[13], B.M. Beadle[14], P. Torres-Saavedra[2], Q-T. Le[15], B. Movsas[16]

[1]Radiation Oncology, The Princess Margaret Cancer Centre/UHN & The University of Toronto, Toronto, ON, Canada; [2]Statistics, NRG Oncology Statistics and Data Management Center, Philadelphia, PA, USA; [3]Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [4]Radiation Oncology, Cleveland Clinic - Cancer Center, Cleveland, OH, USA; [5]Radiation Oncology, University of Wisconsin Carbone Cancer Center, Madison, WI, USA; [6]Otolaryngology Head Neck Surgery, Jamail Specialty Center, Houston, TX, USA; [7]Department of Medicine, UNC - The University of North Carolina at Chapel Hill - School of Medicine, Chapel Hill, NY, USA; [8]Radiation Oncology, Cleveland Clinic Main Campus, Cleveland, OH, USA; [9]Otolaryngology Head Neck Surgery, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [10]Radiation Oncology, OSUCCC - The Ohio State University Comprehensive Cancer Center - James, Columbus, OH, USA; [11]Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA; [12]Radiation Oncology, Fox Chase Cancer Center - Main Campus, Philadelphia, PA, USA; [13]Radiation Oncology, Sutter Cancer Center, Sacramento, CA, USA; [14]Radiation Oncology, Stanford Cancer Center Palo Alto, Palo Alto, CA, USA; [15]Radiation Oncology, Stanford University, Stanford, CA, USA; [16]Radiation Oncology, Henry Ford Cancer Institute-Henry Ford Health, Detroit, MI, USA

Background: This phase 3 randomized non-inferiority de-escalation trial compared cetuximab (cetux) vs cisplatin (cis), concurrent with accelerated RT 70 Gy/6 weeks, in p16+ oropharyngeal cancer (OPC). Quality of life (QOL) was an important secondary endpoint.

Methods: EORTC QLQ-C30/HN35 was completed at baseline, end of treatment, 3, 6, and 12 months post. The substudy aimed for 400 eligible patients. We report completion rates and compare by arm for change from baseline in each domain (0.05 two-sided alpha and MID of 10 points) using linear mixed models.

Results: Consent was 91% (381/419 offered substudy); 6 protocol deviations excluded (n=375). No significant differences in patient/tumor characteristics were found by participation status. Completion rates (%) at the 5 times did not differ by arm (cis/cetux): 92/94, 74/77, 76/81, 76/81, and 73/74. The swallowing domain of HN35 (previously reported) did not differ significantly by arm. No significant difference was seen by arm for the 6-mo change from baseline on any domain. At end of RT (only), dry mouth was significantly worse for RT+cetux. At end of treatment, all domains showed statistically and clinically significant mean worsening across both arms except Emotional Functioning, Dyspnea, Diarrhea, and Teeth. Most domains returned within 10 points of baseline by 6 mo, with the following maintaining significant impairment: Senses (taste/smell), Social Eating, Opening Mouth, Dry Mouth, Sticky Saliva. At 12 mo post-treatment, worsening from baseline persisted for Senses, Dry Mouth, Sticky Saliva, and Weight Gain. Pain Killer use improved significantly from baseline to 3, 6, and 12 mo.

Conclusions: Although replacing RT+cis with RT+cetux did not benefit QOL, this study has confirmed the responsiveness of EORTC QLQ-C30/HN35 to the effects of concurrent systemic/RT for OPC. Dry Mouth, Sticky Saliva, and Senses showed large, significant, and persistent impairments, and remain worthwhile targets for future de-escalation efforts. Domains related to eating (Swallowing, Appetite, Nutritional Supplements, Social Eating, Weight Loss) did not show sustained significant impairment on this instrument in this study.

Clinical trial identification: NCT01302834.

Legal entity responsible for the study: NRG Oncology.

Funding: This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology).

Disclosure: M.L. Gillison: Financial Interests, Personal, Funding, Consulting: Istari Oncology Inc, LLX Solutions, Llc, Kura Oncology, Mirati Therapeutics, BioNtech AG, Shattuck Labs, INC, EMD Serono, INC, Depiopharm, Merck & Co, Ipsen Biopharmaceuticals Inc, Gilead Sciences, Inc, Bristol-Myers Squibb, Bicara Therapeutics, Bayer Healthcare Pharmaceutics, Genocea Biosciences, Inc, Coherus; Financial Interests, Personal, Invited Speaker: OncLive, Roche; Financial Interests, Personal, Advisory Board: Seagen, Sensei Biotherapeutics, Inc; Financial Interests, Personal and Institutional, Research Grant: Genocea Biosciences, Inc, Bristol-Myers Squibb, Genentech, Kura, Cullinan Labs, Agenus; Financial Interests, Personal, Advisory Board, DSMB: SQZBiotech, BioMimetix, Kura. E.M. Sturgis: Non-Financial Interests, Personal, Member of the Board of Directors, also Exec committee of Board: The Immunization Partnership; Non-Financial Interests, Personal, Research Grant: Trinity, Roche Diagnostics. E.M. Basch: Non-Financial Interests, Personal, Member of the Board of Directors: ASCO; Financial Interests, Institutional, Research Grant: NCI, PCORI; Financial Interests, Personal, Funding, consulting: AstraZeneca, Resilience, Sivan, N-Power, Carevive. S.A. Koyfman: Financial Interests, Personal, Advisory Role, consulting: Merck, Regeneron; Financial Interests, Personal, Invited Speaker: Varian; Financial Interests, Personal, Funding, travel expenses: Castle Biosciences; Financial Interests, Personal, Advisory Board, DSMB: Alpha Tau; Financial Interests, Personal and Institutional, Research Grant: BMS, Merck. J.E. Bates: Financial Interests, Personal, Advisory Board: Castle Biosciences, Galera Therapeutics . P. Torres-Saavedra: Non-Financial Interests, Institutional, Research Grant, NRG

Oncology SDMC Grant: US NCI. Q. Le: Financial Interests, Personal and Institutional, Funding, support for group related travel (to NRG retreats): RTOG Foundation; Non-Financial Interests, Personal, Leadership Role, RTOG Group Chair: NRG Oncology. B. Movsas: Financial Interests, Personal, Research Grant: Varian, Philips, ViewRay. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.779

656MO 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

A. Bhatia[1], Z. Chen[2], J. Bruce[3], C.E. Steuer[4], D.P. Zandberg[5], J.W. Riess[6], D. Mitchell[7], T.H. Davis[8], M. Patel[9], V. Kaur[10], S. Arnold[11], T.K. Owonikoko[12]

[1]Medicine, Yale University School of Medicine - Yale Cancer Center, New Haven, CT, USA; [2]Biostatistics, UIC - University of Illinois Chicago - Student Center West, Chicago, IL, USA; [3]Medicine, University of Wisconsin Carbone Cancer Center, Madison, WI, USA; [4]Hematology/Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA; [5]Medicine, University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center, Pittsburgh, GA, USA; [6]Hematology and Oncology, UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [7]Radiation Oncology, OSUCCC - The Ohio State University Comprehensive Cancer Center - James, Columbus, OH, USA; [8]Medicine, Norris Cotton Cancer Center Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [9]Medicine, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [10]Medicine, UVA - University of Virginia - School of Medicine - Division of Hematology & Oncology, Charlottesville, VA, USA; [11]Medicine, UK - University of Kentucky - Markey Cancer Center, Lexington, KY, USA; [12]Department of Medicine, University of Pittsburgh and Hillman Cancer Center, Pittsburgh, PA, USA

Background: M6620 is a highly potent and selective ATP-competitive ATR inhibitor. It showed strong synergy with cisplatin and radiation in preclinical cancer models. The significant vulnerability to ATR inhibition by cancer cells harboring inactivating p53 mutations provided a rationale to test the safety of M6620 along with definitive chemoradiation in Head and Neck Squamous Cell Carcinoma (HNSCC) where such alterations are common.

Methods: Eligible patients with stage III or IV HNSCC not amenable to surgical resection were enrolled in defined dose cohorts using the Escalation with Overdose Control (EWOC) design. The optimal dose of cisplatin (40 or 30mg/m2 weekly) to combine with standard radiation (70Gy) and biologically relevant dose of M6620 (120mg/m2) was tested in stage I. The safety of escalating doses of M6620 across a range of 160 to 280mg/2 along with fixed dose cisplatin and XRT (70Gy) was planned in stage II of the study.

Results: We enrolled 43 patients; median age 60 years (range 45-76); 11.6% Black; 37.2% females. The most common treatment emergent adverse events (TEAE) in 39 evaluable patients were: Anemia (74%), Nausea (72%), Fatigue (69%), Dysphagia (69%), Lymphopenia (69%) and Leukopenia (67%) while the most frequent grade $\geq$3 TEAE occurring in $\geq$ 20% of patients were Lymphopenia (31%), Leukopenia (28%), Anemia (26%), Dysphagia (21%), and Neutropenia (21%). Dose limiting toxicities recorded on study included Dysphagia, neutropenia, thrombocytopenia, febrile neutropenia, intestinal hemorrhage, pseudogout and hypomagnesemia. M6620 was safely combined with cisplatin (40mg/m2) and XRT (70Gy) at doses of 120, 160 and 200mg/m^2. The highest dose of 200mg/m^2 plus standard chemoradiation was declared the recommended phase 2 dose. Unconfirmed best response in 20 evaluable patients by RECIST were complete response (30%), partial response (40%), stable disease (15%) and progressive disease (10%). Ongoing PK and tissue-based biomarker analysis will be presented at the meeting.

Conclusions: M6620 at the dose of 200mg/m^2 was safe and was declared the RP2D in combination with weekly cisplatin (40mg/m2) and standard XRT (70Gy) in locally advanced HNSCC with encouraging initial efficacy.

Clinical trial identification: NCT02567422.

Legal entity responsible for the study: NCI CTEP.

Funding: US National Institutes of Health.

Disclosure: J.W. Riess, T.K. Owonikoko: Financial Interests, Personal, Advisory Board: EMD Serono. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.780

657MO Effectiveness of geriatric assessment-driven interventions on quality of life for 2 years in older patients with head and neck cancer: Results from the EGeSOR trial

C. Lafont[1], E. Paillaud[2], C. Bertolus[3], M. Baron[4], P. Caillet[2], E. Bouvard[5], M. Laurent[6], D. Salvan[7], L. Chaumette[8], L. De Decker Lemarcis[9], B. Piot[10], B. Barry[11], A. Raynaud-Simon[12], E. Sauvaget[13], A. Minard[14], A. Anota[15], H. Panjo[16], L. Brugel[17], F. Canouï-Poitrine[1]

[1]Santé Publique, Univ Paris Est Creteil, INSERM, IMRB, Creteil, France; AP-HP, Hôpital Henri-Mondor, Service de Santé Publique, Créteil, France; [2]Département de Gériatrie, Univ Paris Est Creteil, INSERM, IMRB, Creteil, France; Département de Gériatrie, AP-HP, Paris Cancer Institute CARPEM, Hôpital Européen Georges Pompidou, Paris, France; [3]Service de Chirurgie Maxillo-Faciale, AP-HP, Sorbonne Université, Hôpital Pitié Salpétrière, Paris, France; [4]Service de Soins de Suites et de Réadaptation Gériatrique, AP-HP, Sorbonne Université, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Ivry-sur-Seine, France; [5]Service de Gériatrie, AP-HP, Hôpital Tenon, Paris, France; [6]Département de Gériatrie, Univ Paris Est Creteil, INSERM, IMRB; AP-HP, Hôpital Henri-Mondor, Creteil, France; [7]Service ORL et Cervico-Facial, Centre Hospitalier Sud Francilien, Corbeil-Essonnes, France; [8]Service de Court Sejour Gériatrique, Centre Hospitalier Sud Francilien, Corbeil-Essonnes, France; [9]Service de Gériatrie, Centre Hospitalier Universitaire de Nantes, Nantes, France; [10]Service de Chirurgie Maxillo-Faciale et Stomatologie, Centre Hospitalier Universitaire de Nantes, Nantes, France; [11]Service ORL et Chirurgie Cervico-Faciale, AP-HP, Université de Paris, Hôpital Bichat, Paris, France; [12]Service de Gériatrie, AP-HP, Université Paris Cité, Hôpital Bichat, Paris, France; [13]Service ORL et Chirurgie Cervico-Faciale, Groupe Hospitalier Paris-Saint Joseph, Paris, France; [14]Service de Gériatrie, Hôpital Léopold Bellan, Paris, France; [15]Clinical Research and Innovation Department & Department of Human and Social Sciences, Clinical Research and Innovation Department & Department of Human and Social Sciences, Centre Léon Bérard, Lyon, France; French National Platform Quality of Life and Cancer, Lyon, France; [16]CESP, Université Paris-Saclay, UVSQ, Inserm, Villejuif, France; [17]Service d'ORL et Chirurgie Cervico-faciale, Centre Hospitalier Intercommunal de Créteil, Service d'ORL et Chirurgie Cervico-Faciale, Créteil, France

Background: About 30% of Head and Neck Cancer (HNC) cases are diagnosed in patients aged 70 years and older. Due to their location, HNC and the toxicity of associated treatments may have consequences on quality of life. The aim of this study was to assess the effectiveness of Geriatric Assessment (GA)-driven interventions on quality of life for 2 years in older patients with HNC.

Methods: The EGeSOR study was a two parallel group, multicenter, randomized, controlled and open-label trial, including HNC patients aged 65 years and over between 2013 and 2018. Patients were randomized 1 :1 to receive either a pre-therapeutic GA, a standardized geriatric intervention and follow-up (intervention group) or standard of care (control group). The main outcome was quality of life measures through the European Organisation for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30/100) and HNC questionnaire (QLQ-HN35/100) at 6, 12 and 24 months. Linear mixed models were performed.

Results: Among the 475 patients included (238 in the intervention group and 237 in the control group), the median age was 75.3 years, 31% were women, 44% with oral cancer and 21% metastasis. At baseline, the median score of global health status was 66.7 [50-83.3]. There were no statistically significant differences in evolution between the two groups in either the QLQ-C30 (15 dimensions) or HN35 scores (18 dimensions) over the 24-month period. The evolution of global health status followed a J-shape between M0 and M24 (median gain : 8 points). In the intervention group, 74% of patients did not receive the complete intervention as planned. Statistical analyses regarding age, tumor site and metastasis status are ongoing.

Conclusions: Baseline GA did not improve quality of life for 2 years in older patients with HNC. Difficulties in implementation of complete interventions may have contributed to this result. Alternative models to implement GA-driven interventions could be explored.

Clinical trial identification: NCT02025062.

Legal entity responsible for the study: Assistance Publique des Hôpitaux de Paris - APHP.

Funding: The EGeSOR study was supported by grants from the French National Cancer Institute [INCa] [RAFC1202] and the platform for clinical research in older cancer patients (PACAN, Ligue Nationale contre le Cancer).

Disclosure: E. Paillaud: Financial Interests, Invited Speaker, Honoraria for presentation during an educational Symposium: Amgen, Servier; Financial Interests, Advisory Board: Pfizer, BMS; Financial Interests, Other, Supports for participation to congress, travel and inscription from Nutricia. P. Caillet: Non-Financial Interests, Other, Contract as expert in geriatric oncology for an observational prospective cohort (phase IV). No fees: Pfizer; Financial Interests, Invited Speaker, Honoraria for presentation during an educational Symposium: Amgen; Financial Interests, Advisory Board: Pfizer. A. Raynaud-Simon: Financial Interests, Other: Nestlé, Nutricia, Lactalis, Fresenius, Entreprises de la Nutrition Clinique. A. Anota: Financial Interests, Personal, Advisory Board: Roche, AstraZeneca, Sandoz, Amgen, Ipsen; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Other, Travel fees: BMS, AstraZeneca, Novartis; Financial Interests, Personal, Invited Speaker, Travel fees: AstraZeneca. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.781