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## 869P Results of the multicenter phase II FRAIL-IMMUNE trial evaluating the efficacy and safety of durvalumab (D) combined with weekly paclitaxel carboplatin in 1st-line in patients with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) not eligible to cisplatin

J. Fayette[1], C. Cropet[2], J. Gautier[3], C. Toullec[4], M. Vinches[5], M. Burgy[6], M. Iacob[7], M-C. Kaminsky-Forrett[8], S. Salas[9], B. Linot[10], A. Champagnac[11], I. Sondarjee[2], A. Pechery[12], D. Perol[13], J. Bourhis[14]

*[1]Medicine Dept., Centre Léon Bérard, Lyon, France; [2]Clinical Research Department, Centre Léon Bérard, Lyon, France; [3]Rhône, Centre Léon Bérard, Lyon, France; [4]Medicine Dept., Institut Sainte-Catherine, Avignon, France; [5]Medical Oncology Department, ICM - Institut du Cancer de Montpellier, Montpellier, France; [6]Medical Oncology Department, ICANS - Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [7]Oncology Department, Gustave Roussy - Cancer Campus, Villejuif, France; [8]Medical Oncology Unit, Institut de Cancérologie de Lorraine - Alexis Vautrin, Vandoeuvre-lès-Nancy, France; [9]Oncology, AP-HM - CHU La Timone Enfants, Marseille, France; [10]Hôpital Privé du Confluent, Nantes, France; [11]Biopathology department, Centre Léon Bérard, Lyon, France; [12]Clinical Research Department, GORTEC, Tours, France; [13]Clinical Research Department, Centre Léon Bérard, Lyon, France; [14]Radiation Oncology Department, CHUV - Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*

**Background:** For patients (pts) with R/M SCCHN, standard of care is pembrolizumab (P) either alone or combined with platin-5FU (KN 048 — median Overall Survival (OS): 13 months when combined). Pts who cannot receive platinum-5FU are treated by P alone or chemotherapy (CT) in monotherapy, with a poor OS. This population is generally excluded from clinical trials. After clinically significant results in patients with Performance Status (PS) $\leq$1, we investigated the efficacy and tolerance of PD-L1 inhibition with D combined with weekly carboplatin-paclitaxel as 1st-line in frail R/M SCCHN pts with PS2.

**Methods:** This single-arm phase II enrolled pts in 1st-line of their R/M SCCHN, not eligible to cisplatin-based CT, with a PS2. Pts received 4 CT cycles (carboplatin AUC2; paclitaxel 80mg/m$^2$ both at D1, D8, D15) and D 1500mg repeated every 4 weeks up to 12 months. The primary endpoint was OS rate at 12 months (m). The study used a A'Hern design (inefficacy boundary: 15% and target efficacy: 35%), requiring 10 successes among 38 pts. Main secondary endpoints were Progression-Free Survival (PFS), objective response rate (ORR) and tolerance.

**Results:** 40 pts (median age 67.0y; 90.0% males) with PS2 were included, regardless of their PD-L1 status. Primary tumors were mainly located in oral cavity (40.0%) and oropharynx (35.0%) with 45.7% PD-L1 CPS$>$20. 50.0% were metastatic. The efficacy rule for OS was met with 20 pts (51.3%, unilateral 95%CI: [37.1%; - ]) alive at 12m among the 39 evaluable pts. With a median follow-up of 24.7 m, median OS was 12.4 m (95% CI [6.7 — 22.6]) and the 24m-OS rate was 29% [14%-45%]. Median PFS was 5.3 m (95% CI [3.7-7.2]). 23/38 pts (60.5%) achieved an OR (2 complete responses and 21 partial responses). 15.0% of pts experienced G$\geq$3 D-related adverse events. Toxicity led to permanent discontinuation of D in 7.5% of pts. 3 SUSAR were reported (death of unknown cause).

**Conclusions:** The combination of D with weekly carboplatin/paclitaxel confirms its efficacy and good tolerance in 1st-line R/M SCCHN and appears as an appropriate option for frail patients with PS2.

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**Funding:** AstraZeneca.

**Disclosure:** J. Fayette: Financial Interests, Personal, Advisory Board: AstraZeneca, MSD, Innate Pharma, Merck Serono, Roche, Pfizer, Hookipa; Non-Financial Interests, Principal Investigator: AstraZeneca, MSD, Pfizer, Meru, Calliditas, Isa. C. Toullec: Financial Interests, Personal, Invited Speaker: Amgen, BMS, MSD, Pierre Fabre, Viatris; Financial Interests, Personal, Advisory Board: Bayer, Merck Serono, Sanofi, Servier, AstraZeneca, Oncoscience. D. Perol: Financial Interests, Personal, Invited Speaker: AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Gilead, Ipsen, Pfizer, Novartis, Merck Sharp And Dohme, Roche, Takeda; Financial Interests, Personal, Advisory Board: Brenus Pharma; Other, Travel Expenses (ESMO Annual Meeting Madrid 2023): Novartis; Other, Travel Expenses (ESMO Annual Meeting Paris 2022): Roche. All other authors have declared no conflicts of interest.

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## 870P POPPY: A phase II trial to assess the efficacy and safety profile of pembrolizumab in patients of performance status 2 with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M HNSCC)

M.D. Forster[1], J. Mason[2], R. Moleron[3], J.J. Sacco[4], M. Beasley[5], M. Reis Ferreira[6], D. Srinivasan[7], K. Yip[8], G. Stewart[9], K. Chiu[10], A. Ward[11], R. Metcalf[12], T. Adedoyin[13], R. Begum[14], M. Chiwewe[13], K. Poole[13], V. Spanswick[15], Y. Pathak[15], N. Counsell[16], M.K. Rashid[17]

*[1]Oncology, University College London Cancer Institute/University College London Hospitals NHS Trust, London, UK; [2]Oncology, Musgrove Park Hospital - Taunton and Somerset NHS Foundation Trust, Taunton, UK; [3]Oncology, Aberdeen Royal Infirmary - NHS Grampian, Aberdeen, UK; [4]Medical Oncology Department, Clatterbridge Cancer Center - NHS Foundation Trust, Wirral, UK; [5]Oncology, BHOC - Bristol Haematology and Oncology Centre, Bristol, UK; [6]Oncology, KCL - King's College London, London, UK; [7]Oncology, Edinburgh Cancer Centre, Western General Hospital, Edinburgh, Sheffield, UK; [8]Oncology, Ipswich Hospital - East Suffolk and North Essex NHS Foundation Trust, Ipswich, UK; [9]Oncology, Royal Cornwall Hospital - Royal Cornwall Hospital Trust NHS Trust, Truro, UK; [10]Oncology, Mount Vernon Cancer Centre, Northwood, UK; [11]Oncology, Queen's Hospital - Barking, Havering and Redbridge University Hospitals - NHS Trust, Romford, UK; [12]Medical Oncology Dept., The Christie NHS Foundation Trust, Manchester, UK; [13]Cancer Research UK & University College London Cancer Trials Centre, UCL Cancer Institute - UCL-London's Global University, London, UK; [14]Cancer Research UK & UCL Cancer Trials Centre, Cancer Research UK & University College London Cancer Trials Centre, London, UK; [15]UCL ECMC GCLP Facility, UCL Cancer Institute - UCL - London's Global University, London, UK; [16]Cancer Institute, Cancer Research UK & University College London Cancer Trials Centre, London, UK; [17]Statistics, Cancer Research UK & University College London Cancer Trials Centre, London, UK*

**Background:** Pembrolizumab, with or without chemotherapy is a standard treatment for fit patients with R/M HNSCC, with median survival of 8-11 months. Pembrolizumab alone has a response rate of ~15% in PD-L1 unselected patients. However, many patients with R/M HNSCC are not fit and there is no accepted standard of care these patients, who have a median survival of 3-6 months with best supportive care alone.

**Methods:** POPPY (NCT03813836) is a UK multicentre single-arm phase II trial in patients with R/M HNSCC and a WHO Performance Status (PS) of 2. Patients receive pembrolizumab 200 mg intravenously every 3 weeks, for up to 24 months. Primary endpoint is disease control rate (DCR) at 24 weeks, using iRECIST. 59 patients are required to detect a disease control rate (DCR) $\geq$20% and exclude an unacceptable DCR $\leq$10%, with 85% power and one-sided 15% significance level. Secondary endpoints include toxicity, response, progression-free survival (PFS) and overall survival (OS). Blood and tissue are collected for exploratory translational studies.

**Results:** 63 patients were recruited from 12 UK centres (Aug 2019 — Aug 2023). 57 patients received pembrolizumab, median 4.5 cycles (range: 1-32). Treatment-related adverse events were observed in 31 (54.4%), with grade 3 or higher events seen in 9 patients (15.8%; 1 grade 4 colitis, no grade 5 events). 54 patients were eligible and evaluable for disease response. DCR at 24 weeks was 27.8% (95%CI:16.5-41.6), exceeding the unacceptable DCR rate of 10%. The overall response rate was 31.5% (17/54; 95%CI:19.5-45.6), with a median PFS of 4.0 (95%CI:2.1-5.7) and OS of 7.6 (95%CI:6.7-10.6) months respectively.

**Conclusions:** POPPY is the first prospective study to evaluate pembrolizumab in PS2 patients with R/M HNSCC. It demonstrates meaningful anti-tumor activity, with no signals of increased toxicity; this is particularly encouraging as the observed results are consistent with studies in fitter patients.