Background Management of patients with recurrent endometrial cancer after failure of platinum therapy remains an important clinical challenge. Tumors characterized by abnormalities in DNA repair are associated with high numbers of neoantigens, making immunotherapy a promising approach. Retifanlimab (INCMGA00012) is an investigational humanized immunoglobulin G4 monoclonal antibody against PD-1. In the dose escalation and tumor expansion portions of the POD1UM-101 phase 1 study, retifanlimab monotherapy demonstrated acceptable tolerability and durable clinical activity in multiple advanced tumor types, including pretreated endometrial cancer. Here we present interim clinical activity and safety data from a preplanned futility assessment in patients with microsatellite instability-high (MSI-H) recurrent endometrial cancer.

Methods Patients eligible for this cohort had histologically proven, unresectable recurrent endometrial cancer that was MSI-H or deficient mismatch repair (dMMR) based on local testing (either by PCR or IHC), ECOG performance status (PS) ≤ 1, disease progression during or following ≤ 5 prior systemic treatments, measurable disease per RECIST v1.1, and no prior treatment with immune checkpoint inhibitors. The primary endpoint is safety (using CTCAE v4.03 grading). Confirmed best overall response rate and duration of response were evaluated by RECIST v1.1 (investigator’s assessment). Retifanlimab 500 mg Q4W was administered up to 2 years.

Results As of April 7, 2020, 44 patients who received at least 1 dose of retifanlimab were assessed for safety, including 24 patients who were fully assessable for the planned futility analysis. Median age was 63 (49–86) years, 45.5% had an ECOG PS of 1, and 97.7% had adenocarcinoma (1 had missing histology data at cut-off). Of the 44 patients treated, all but 1 were pretreated with at least 1 prior platinum-based chemotherapy, 72.7% were treated with radiotherapy, and 90.9% underwent surgery. Median drug exposure was 1.9 (0.03–11.1) months. Eight patients (18.2%) experienced Grade (G) 3/4 AEs regardless of causality with anemia being the leading event (n=3, 6.8%). Two patients (4.5%) had immune-related AEs (n=1 each: dry mouth [G3] and myositis [G3]); both patients discontinued study treatment because of the event. No treatment-related deaths occurred. Confirmed responses (7 PR, 1 CR) per RECIST v1.1 were observed, supporting study continuation. Median duration of response was not reached, as no confirmed responders had disease progression or died at time of this analysis.

Conclusions Retifanlimab was generally well tolerated with preliminary evidence of encouraging antitumor activity in MSI-H pretreated advanced endometrial cancer. Enrollment is ongoing.

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Trial Registration NCT03059823, EudraCT 2017-000865-63

Ethics Approval The study was approved by institutional review boards or independent ethics committees of participating institutions.

Consent n/a

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269 TUMORAL AND PERIPHERAL LANDSCAPE OF VIRAL-VERSUS CARCINOGEN-DRIVEN HEAD AND NECK CANCER

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Background Head and neck squamous cell carcinoma (HNSCC) is composed of a heterogeneous group of tumors arising through environmental carcinogens or infection by human papillomavirus (HPV). Treatment interventions such as immunotherapy and targeted therapy have shown clinical benefit in HNSCC patients. Despite these encouraging results, resistance to treatment is still observed in the majority of patients. Additionally, clinical effectiveness of treatment options has also been shown to be associated with HPV status. Here we investigate the tumoral and peripheral landscape of HPV(-) vs. HPV(+) head and neck cancers to identify features able to expand treatment options for patients with Viral- and Carcino-nogen-Driven Head and Neck Cancer.

Methods Biopsies and serum samples derived from 502 primary and metastatic HNSCC patients were leveraged for genomic, proteomic and immunochemistry evaluations. Tumor biopsies from HNSCC patients commercially obtained (n=143) or derived from patients enrolled in CP1108 trial (n=19, NCT01693562) were profiled by gene expression. Primary tumor biopsies (N=198) from HNSCC have been assessed by Whole Exome Sequence (WES). Expression of immune markers including CD8, Nkp46 was evaluated by immunohistochemistry (IHC) on 186 and 214 tumors biopsies, respectively. The expression of 80 immune related soluble factors was evaluated in serum derived from n=285 patients of HNSCC enrolled in EAGLE (NCT02369874), a randomized, open-label, study assessing Durvalumab and Tremelimumab vs. Standard of Care (SoC). Statistical comparison between HPV (+) vs. HPV (-) samples were conducted using R software.

Results Patients with HPV(-) vs. HPV(+) HNSCC were characterized by worse prognosis. Increased levels of immunosuppressive factors including VEGF (p=0.01), IL-8 (p=0.02), IL6 (p=0.07) and macrophages chemo attractive factor CCL4 (p=0.07) was observed in the serum of HPV(-) vs HPV(+) HNSCC patients. In the tumor microenvironment, higher mRNA expression of immune signatures associated with MDSC, Cancer Associated Fibroblast (CAF), and Metalloproteinase (MMP) was observed in HPV(-) vs. HPV (+) HNSCC patients. In contrast, HNSCC HPV(+) patients were characterized by increased mRNA expression of DC signatures and IFNγ related genes (i.e. CXCL9). No differential infiltration of T and NK cells (CD8+ and Nkp46+) were found in HPV(-) vs. HPV(+) patients. Enrichments of mutations in EGFR, and DNA repair genes (PMS1, POLK, ATM) was observed in HPV(+) patients. On the contrary, enrichments of mutations in TP53 was observed in HPV(-) patients.

Conclusions Deep evaluation of tumoral and peripheral landscape of viral- versus carcinogen-driven HNSCC might help understanding differential outcome of treatments regimens in HPV(+) vs HPV (-) HNSCC thus leading to novel therapeutic interventions.

Trial Registration NCT01693562, NCT02369874

Ethics Approval The study was approved by Astrazeneca.
Abstracts

Consent Patients provided written consent to perform evaluations here described.

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**271 CONSISTENT HIGH-QUALITY DENDRITIC CELL VACCINES PRODUCED POST-CHEMOTHERAPY IN PATIENTS WITH ACUTE MYELOID LEUKEMIA FOR USE IN A PHASE III TRIAL**

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Background A Phase III/II dendritic cell (DC) vaccine trial was completed in 20 patients with acute myeloid leukemia (AML) in complete remission or CRi after chemotherapy who were ineligible for hematopoietic stem cell transplantation (NCT02405338). The DC vaccines were designed to delay disease progression by mobilizing natural killer (NK) cells through secretion of IL-12(p70) and activating T cells by stimulation with WT-1 and PRAME, two prominent antigens in AML. DC vaccination was carried out in weeks 1, 2, 3, 4, 6 and monthly thereafter for 2 years. Two questions were prominent at the trial start. First, could mature DCs (mDCs) be efficiently prepared to accommodate the vaccine regimen, including use of separate DC-fractions for each antigen. Second, could suitable quality DC vaccines be generated from patients with myeloid disease, since all had received intensive chemotherapy, impairing hematopoiesis, such that several patients showed extended times for monocyte recovery in peripheral blood before being able to undergo apheresis for production.

Methods Immune monitoring tools were used to assess DC vaccines: multi-color flow cytometry for surface and intracellular protein staining, dual-color ELISpot for secretion of IL-10/IL-12, and chemokine-directed trans-well migration. Detection of delayed type hypersensitivity responses post-vaccination at six weeks indicated the patient groups that relapsed or remained in remission. mDCs/antigen/ampule) to be completed. In 15/20 patients one other treatment cycle, each intravenously administered weekly. Patients underwent 1-month safety assessment post the 4th infusion, according to Common Terminology NCI CTCAE Version 4.0.3. If there were no dose associated toxicities, patients were eligible to continue administration of LioCyx-M at dose of 5 × 10^6 cells/kg BW weekly. Tumor response per RECIST 1.1 criteria and survival time were assessed.

Results At data cutoff (30 April 2020), eight patients were enrolled, with a median age of 53 (range: 49 - 67). These patients received a median number of 6 (range: 4 - 12) infusions of LioCyx-M. 1 patient developed Grade 3 elevations in alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST) and bilirubin after the first treatment cycle, each intravenously administered weekly. Patients underwent 1-month safety assessment post the 4th infusion, according to Common Terminology NCI CTCAE Version 4.0.3. If there were no dose associated toxicities, patients were eligible to continue administration of LioCyx-M at dose of 5 × 10^6 cells/kg BW weekly. Tumor response per RECIST 1.1 criteria and survival time were assessed.

Conclusions DC vaccine production feasibility was clearly fulfilled and high quality mDCs were generated for every patient. Quantity and quality of DC vaccines did not differ in the patient groups that relapsed or remained in remission, nor in patients who succumbed to disease during the trial. DC vaccines were remarkably consistent, although originating from patients differing in age, AML subtype and receiving varied amounts of standard chemotherapy regimens.

Ethics Approval The study was approved by the responsible Norwegian ethics committee, approval number 2014/1677.

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**272 USE OF LIOCYX-M, AUTOLOGOUS HEPATITIS B VIRUS (HBV)-SPECIFIC T CELL RECEPTOR (TCR) T-CELLS, IN ADVANCED HBV-RELATED HEPATOCELLULAR CARCINOMA (HCC)**

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Background We have demonstrated the ability of Hepatitis-B-virus (HBV)-specific T cell receptor (TCR) bioengineered T cells to recognize and lyse Hepatocellular carcinoma (HCC) cells expressing HBV antigens derived from HBV-DNA integration in patients with liver transplant. LioCyx-M is an immunotherapeutic product composed of autologous T cells transiently modified with *in-vitro* transcribed mRNA encoding HBV-specific TCR. The transient TCR expression makes LioCyx-M amenable to a dose escalating posology.

Methods The primary endpoint of this phase 1 trial is to assess the safety and tolerability of LioCyx-M in patients with advanced HBV-HCC without curative treatment options. Eligible patients were diagnosed with Barcelona clinic liver cancer stage B or C HCC (Child-Pugh < 7 points), receiving >1 year antiviral treatment prior to enrollment. These patients had matching HLA class I genotypes which present HBV encoded antigen. Peripheral blood was collected from each patient prior to each dose for LioCyx-M manufacturing. Patients received 4 escalating doses of 1×10^4 cells/kg, 1×10^5 cells/kg, 1×10^6 cells/kg, 5×10^6 cells/kg bodyweight (BW) in the first treatment cycle, each intravenously administered weekly. Patients underwent 1-month safety assessment post the 4th infusion, according to Common Terminology NCI CTCAE Version 4.0.3. If there were no dose associated toxicities, patients were eligible to continue administration of LioCyx-M at dose of 5 × 10^6 cells/kg BW weekly. Tumor response per RECIST 1.1 criteria and survival time were assessed.

Results At data cutoff (30 April 2020), eight patients were enrolled, with a median age of 53 (range: 49 - 67). These patients received a median number of 6 (range: 4 - 12) infusions of LioCyx-M. 1 patient developed Grade 3 elevations in ALT, GGT, AST and bilirubin after receiving LioCyx-M at dose level of 1×10^5 cells/kg BW. Another patient had Grade 1 transient fever after receiving LioCyx-M at dose level 5×10^6 cells/kg BW in the 4th, 5th and 6th infusions. No treatment-related adverse events (trAEs) such as cytokine release syndrome or neurotoxicity were observed. No fatal trAEs were observed. The median time to progression was 1.9 months (range: 0.2 - 9.5 months). The median overall survival was 34 months (range: 3 - 38.2 months).

Conclusions The encouraging clinical outcome and tolerable safety highlight the good benefit-risk profile of LioCyx-M. Therefore, further exploration of efficacy of LioCyx-M treatment for advanced HBV-HCC is warranted in a Phase 2 proof-of-concept clinical study.

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Trial Registration NCT03899415

Ethics Approval The study was approved by Fifth Medical Center of Chinese PLA General Hospital’s Ethics Board, approval number R2016185D1010.