## 790 PHASE I CLINICAL TRIAL ON INTRATUMORAL ADMINISTRATION OF AUTOLOGOUS CD1C (BDCA-1)$^+$/ CD141 (BDCA-3)$^+$ MYELOID DENDRITIC CELLS PLUS IPILIMUMAB AND AS01$_B$ IN COMBINATION WITH INTRAVENOUSLY ADMINISTERED NIVOLUMAB

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**Background** The presence of CD1c (BDCA-1)$^+$ (cDC2) and CD141 (BDCA-3)$^+$ (cDC1) conventional dendritic cells (myDC) in the tumor microenvironment (TME) is a necessary prerequisite to induce an effector CD8$^+$ T cell response and for response to immune checkpoint blockade (ICB).[1-4] AS01$_B$ is an adjuvant component of a commercialized prophylactic shingles vaccine which induces adaptive immunity through recruitment and activation of cDC1 and cDC2.[5-6] Previously, intratumoral (IT) administration of ipilimumab and autologous myDC has shown promising antitumoral activity.[7]

**Methods** In this phase Ib clinical trial, patients with metastatic melanoma refractory to ICB and BRAF/MEK inhibitors (in case of BRAF V600-mutant melanoma) were recruited. Patients underwent a leukapheresis followed by immunomagnetic bead isolation of CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC. Patients received an intravenous (IV) administration of low dose nivolumab (10mg d1 and q2w) plus an IT administration of ipilimumab 10 mg (d1 and q2w). The isolated myDC were injected (palpation or ultrasound-guided) as a single injection into a metastatic lesion on day 2; together with AS01$_B$0.5 ml (d2 and q2w). Response assessment was performed by PET/CT q12w. Blood and tissue samples were collected each treatment cycle. Translational research including gene expression profiling, TCR analysis and multiplex immunohistochemistry is ongoing. (figure 1)

**Results** Between July 2021 and May 2022, 8 patients were recruited (all female) with a median age of 63 years (range 33-83). All patients had been treated with ICB as well as BRAF/MEK inhibitors when applicable. Median number and range of treatment administrations was 4 (range 1-7) for IT and 4.5 (range 1-15) for IV. Three patients remained on treatment at data cutoff date. Median PFS was 10.1 weeks (95% CI 5.193-15.007), median OS has not been reached. One patient obtained a complete remission on PET/CT 6 months after the start of study treatment. One patient obtained a pathological complete response 4 weeks after start of study treatment. One patient obtained a complete remission of injected lesions but progressed in non-injected lesions. Three patients died due to progressive disease. Treatment was well tolerated. There were no unexpected adverse events. One patient had G3 pyrexia, leading to prolongation of hospital stay with 1 day.

**Conclusions** In this clinical trial, IT injection of CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC in combination with repeated IT administration of ipilimumab and AS01$_B$ and systemic low dose nivolumab has shown promising early results and no unexpected safety signals, deserving further clinical investigation. Translational investigations are ongoing.

**Trial Registration** Clinicaltrials. gov: NCT03707808

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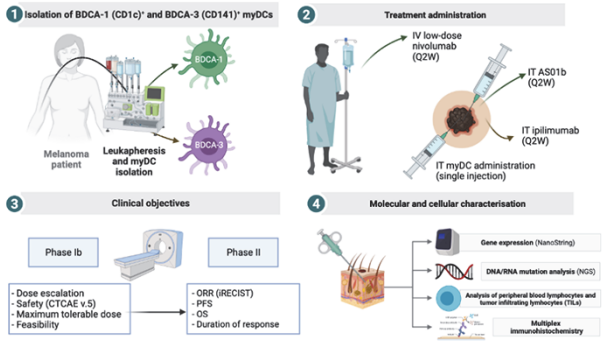
**Ethics Approval** Clinical trial protocol was approved by the medical ethics committee of Universitair Ziekenhuis Brussel and by the Belgian Federal Agency for Medicines and Health Products. Patients have signed an informed consent for participation in this clinical trial.

**Consent** Written consent of participating patients was obtained for publication of anonymized patient data. A copy of the written consent is available for review by the Editor of this journal.




**Abstract 790 Figure 1** Schematic overview of clinical trial (Created in Biorender.com)

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