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# A phase I clinical trial on intratumoral injection of autologous CD1c (BDCA-1)+/CD141 (BDCA-3)+ myeloid dendritic cells (myDC) in combination with talimogene laherparepvec (T-VEC) in patients with advanced pretreated melanoma

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## Background

Intratumoral (IT) myDC play a pivotal role in initiating antitumor immune responses within the tumor microenvironment. IT injection of the oncolytic virus T-VEC may lead to the release of tumor antigens and maturation signals that can be captured and processed by CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC, thereby reinvigorating the cancer immunity cycle.

## Methods

Patients (pts) with ICI-refractory melanoma received IT injections of ≥1 non-visceral metastases with T-VEC ($10^6$ PFU/mL; max 4 mL) on day 1 followed by IT injection of CD1c (BDCA-1)$^+$ (cohort C1) or CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC (cohort C2) on day 2. Injection of T-VEC ($10^8$PFU/mL; max 4 mL) was repeated on day 21, and Q2w thereafter. In C1, the number of CD1c (BDCA-1)$^+$myDCs was escalated from $0.5x10^6$, to $1x10^6$, and $10x10^6$ cells. In C2, pts received all isolated CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDCs. Primary objectives were safety and feasibility. Immunohistochemistry (IHC), gene expression profiling (GEP), and multiplexed immunofluorescence (mIF) of baseline and on-treatment biopsies was performed.

## Results

13 pts were enrolled (C1: n=7 [respectively 2, 2, and 3 pts per dose-level of myDC]; C2: n=6). Pts received the predefined dose of myDCs and a median of 6 (range 3-8) T-VEC injections. Most frequent AEs were fatigue in 11 pts (85%), injection-site pain in 9 pts (69%), fever in 8 pts (62%), and chills and flu-like symptoms in 6 pts (46%). There were no G4 or G5 AEs. AEs of special interest were a G3 eosinophilia and a G2 purpuric rash at the injection-site; 2 pts (C1, dose level 3) developed a pathological complete remission that is ongoing at 24 months following treatment initiation. One pt in C2 had an unconfirmed partial response (iRECIST); a mixed response was observed in 2 pts. Responses were observed in both injected and non-injected lesions. In responder pts, infiltration of lymphocytes was observed on IHC. GEP and mIF on biopsies are ongoing.

## Conclusions

IT co-injection of CD1c (BDCA-1)$^+$ +/- CD141 (BDCA-3)$^+$ myDC plus T-VEC is feasible, tolerable, and resulted in encouraging early signs of durable antitumor activity in pts with ICI-refractory melanoma.

## Clinical trial identification

NCT03747744.

## Legal entity responsible for the study

Department of Medical Oncology, Universitair Ziekenhuis Brussel.

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## Disclosure

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