

## Phase II study of Interleukin-21 in patients with metastatic or recurrent melanoma.

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*Aims:* To evaluate the efficacy, toxicity, pharmacokinetics, immunogenicity and biomarker profile of Interleukin-21 (rIL-21) in a multicentre phase II study of patients with metastatic melanoma (MM).

*Methods:* Patients with no prior systemic therapy for MM were treated with rIL-21 using 3 different dosing regimens. The initial cohort received 50µg/kg/day by outpatient intravenous bolus injection daily x 5, every other week x 3 q 8 weeks. Cohort 2 received 30µg/kg/day in the same schedule and Cohort 3 received 50µg/kg/day daily x 5 every other week x 2 q 6 weeks. The primary endpoint was objective response rate with molecular correlates on archival melanoma as a secondary endpoint.

*Results:* As of January 5, 2009 22 patients have been treated: 3 in cohort 1, 16 in cohort 2 and 3 in cohort 3. Archival tissue has been retrieved in 21 patients. The median age was 52 years and majority of patients had multiple sites of disease. The median number of cycles received was 2 (range 1-4). Five patients had a partial response (one not yet confirmed) (23%) and 9 (41%) have stable disease. Of the 3 patients in the 1<sup>st</sup> cohort, 2 had a dose limiting toxicity (DLT) of complicated grade 4 neutropenia thus the subsequent 16 patients in this schedule were treated at 30µg/kg/day. The protocol was subsequently amended for the third cohort to evaluate 50 µg/kg/day with only two 5-day cycles. Overall, five patients had grade 3 rash and grade 1 or 2 fatigue and muscle pain were common.

*Conclusions:* The preliminary response rate to rIL-21 for first-line MM is 23% and warrants further investigation and dose optimization. The study is currently accruing to both cohort 2 and 3 and correlative studies including tumour expression of IL21 receptor are ongoing.