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Abstract

Objective: Interleukin-21(IL-21) is a T-cell derived cytokine with antitumour activity dependent on NK cells or CD8+ T cells. A previous phase II study demonstrated an overall response rate (ORR) of 22.5% in previously untreated patients with metastatic melanoma. We conducted a multi-centre randomized phase II study in metastatic melanoma patients to evaluate the efýcacy, toxicity, immunogenicity and biomarkers associated with response to IL-21 versus dacarbazine (DTIC).

Methods: Eligible patients: Recurrent, non-resectable or metastatic melanoma patients were treated with either IL-21, 30 Ôg/kg/day dose intravenous (IV) daily x 5 days, weeks 1, 3, 5, q 8 weeks or dacarbazine (DTIC) 1000 mg/m2 IV day 1, q 3 weeks. The primary objective was to compare progression free survival (PFS).

Results: 64 patients were randomized, 32 in the IL-21 arm and 32 in the DTIC arm. In the treated population, PFS (1.87 months for IL-21, 2.04 months for DTIC) and ORR {IL-21: 13.3% (95% CI: 3.8 to 30.7), DTIC: 14.3% (95% CI: 4.0 to 32.7)} was similar in both groups. Most common adverse events (AEs) in Arm 1 (IL-21) were nausea (38%), fatigue (56%), fever (34%), maculo-papular rash (34%), and pruritis (38%). In Arm 2 (DTIC) the most common AEs were fatigue (39%), constipation (29%), and nausea (21%). Biomarker studies showed no correlation of sCD25 changes and PFS outcome (HR=0.86, 95% CI. 0.73 to 1.02).

Conclusions: Despite encouraging efýcacy in prior phase I/II studies, the results suggest that IL-21 is comparable to DTIC in this speciýc patient population.

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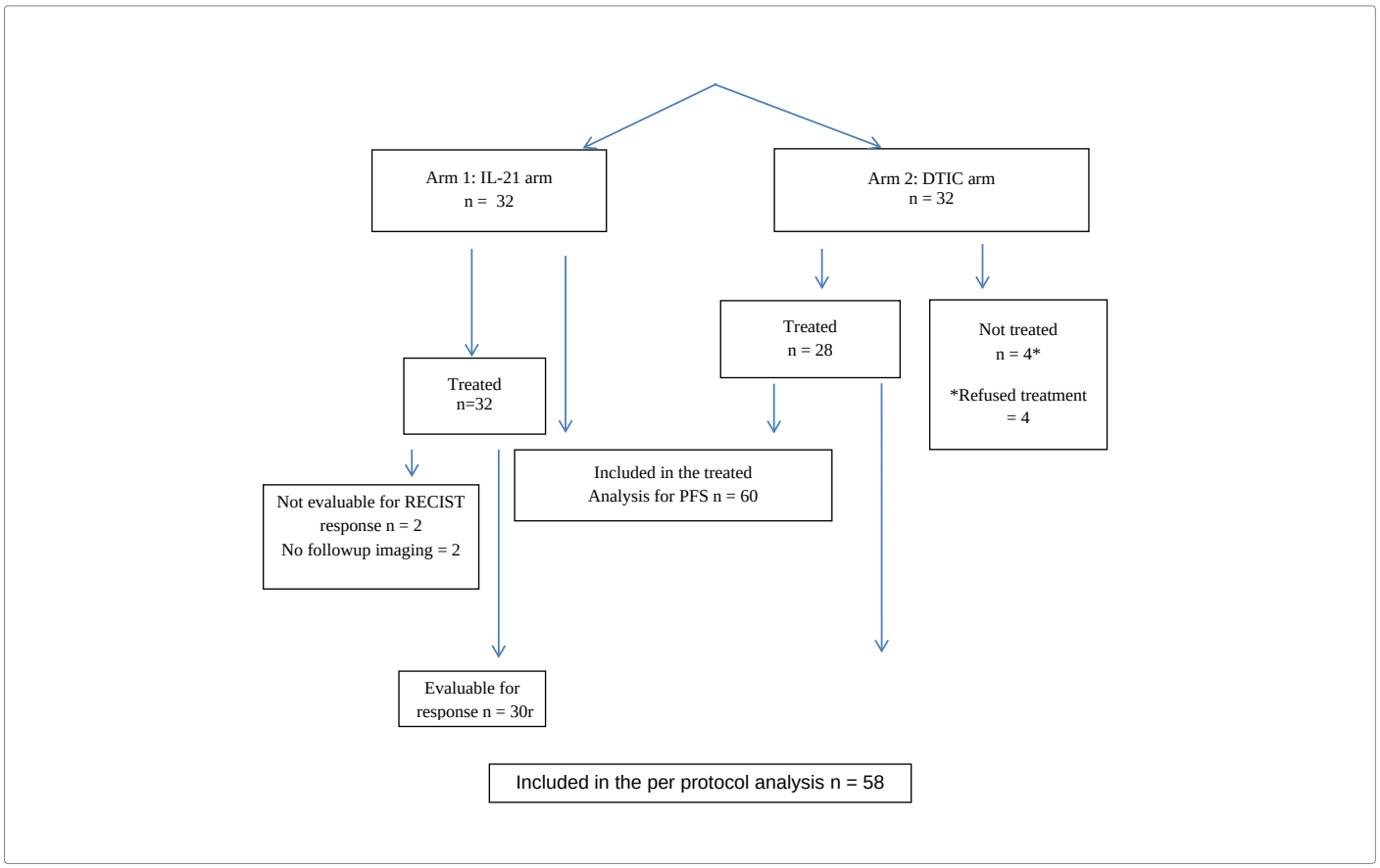
Patients and Methods

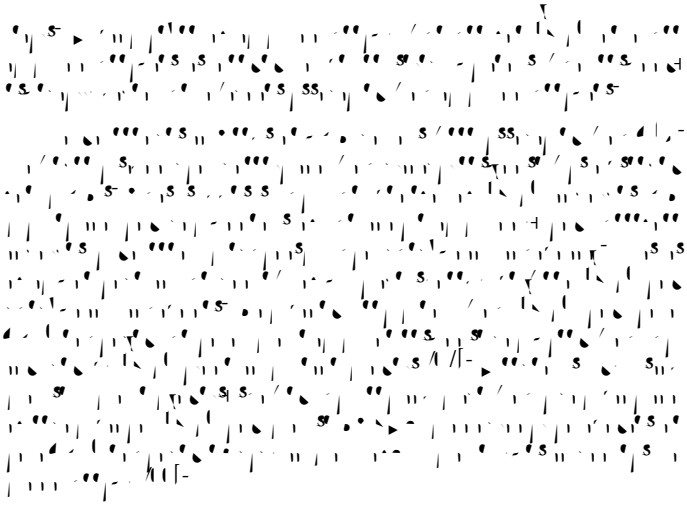
Patients

Study design

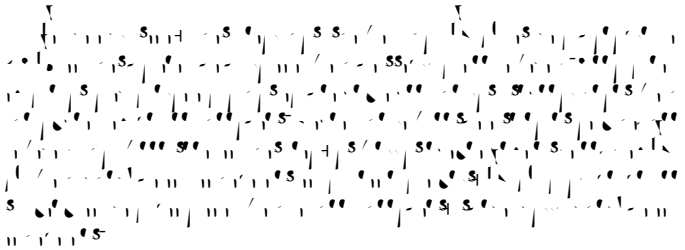


Primary e cacy endpoint

Secondary e cacy endpoints



Conclusion



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