GDA-201, NICOTINAMIDE (NAM) EXPANDED NK CELLS DERIVED FROM PERIPHERAL Apheresis, SHOW UNIQUE CULTURE KINETICS AND INCREASED EXPANSION

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Background Nicotinamide (NAM), an allosteric inhibitor of NAD-dependent enzymes, is a master regulator of NAD-related signaling pathways. Ex-vivo expansion of Natural Killer (NK) cells using Gamida-cell’s proprietary nicotinamide platform enhances NK cellular functionality and phenotype, and improves homing and retention to lymphoid tissues. Gamida Cell has developed a reliable, scalable and GMP-compliant culture method for NAM expansion that yields highly functional NK cells. Clinical responses were observed in a Phase 1 trial of patients with refractory non-Hodgkin lymphoma (NHL) treated with a fresh formulation of GDA-201 (Bachanova Blood 2019;134:777). A ready to use, cryopreserved formulation of GDA-201 is currently being evaluated in a multicenter Phase 1/2 clinical trial in patients with NHL (NCT05296525). We have previously described the unique, non-exhausted and immature phenotype of GDA-201 NK cells. This study aims to gain deeper insight into NAM-NK culture kinetics and the contribution of NAM to the robustness of the manufacturing process.

Methods A total of ten batches of NK culture were manufactured using an apheresis unit from a healthy donor. CD3-cells were isolated, seeded in the presence of irradiated CD3+ ‘feeder’ cells from the same donor, and cultured for 14 days with interleukin (IL)-15 with or without NAM. The impact of NAM on cell expansion and proliferation was tested. Fold expansion of culture with or without NAM were compared at harvest day.

Results NK cells cultured with NAM showed higher fold expansion (68.7±15.3 SEM) than culture without NAM (44.8±13.3 SEM ). The higher fold expansion persisted up to 21 days. Examination of cell identity revealed that NAM prolonged the survival of feeder cells on the first days of expansion (45% on day 2–3 compared to number seeded), while feeder cells survival decreased dramatically in the absence of NAM (13% on day 2–3 compared to number seeded).

Conclusions These data provide further evidence for the unique characteristics of NAM-NK, resulting in increased cell proliferation and robustness of the manufacturing process.

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