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Macrophage derived immunotherapy in glioblastoma: Phase I TEM-GBM-001 results

F. Ciceri[1], F. Farina[1], B. Gentner[2], M. Eoli[3], M. Barcella[4], E. Anghileri[3], Q.G. D'alessandris[5], V. Ferla[1], A. Franzin[6], F. Gagliardi[7], F. Legnani[3], A. Capotondo[8], S. Mazzoleni[8], A. Olivi[5], R. Pallini[5], M. Saini[3], S. Snider[7], L. Naldini[4], C. Russo[9], G. Finocchiaro[10]

[1] Hematology and Bone Marrow Transplant Unit, IRCCS Ospedale San Raffaele, Milano, Italy, [2] Oncology Department, UNIL CHUV Ludwig Institute for Cancer Research, Lausanne, Switzerland, [3] Department of Neuro-Oncology, Fondazione IRCCS - Istituto Neurologico Carlo Besta, Milano, Italy, [4] SR-Tiget, San Raffaele Telethon Institute for Gene Therapy, Milano, Italy, [5] Neuroscienze, Organi di Senso e Torace, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [6] U. O. Neurochirurgia, Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy, [7] Neurosurgery Unit, IRCCS Ospedale San Raffaele, Milano, Italy, [8] R&D, Genenta Science Spa, Milano, Italy, [9] Genenta Science, New York, NY, USA[10] Neurology Department, IRCCS Ospedale San Raffaele, Milano, Italy

Background

Glioblastoma (GBM) is an incurable glial tumor affecting the CNS. The reported historical median survival in the unfavorable patients' subgroup with unmethylated MGMT promoter is 12.7 months with less than 15% of patients surviving up to 2 years. Despite immunotherapies being able to slow or eradicate numerous tumors, none so far have extended survival in GBM.

Methods

We are concluding Phase I of a dose-escalating, open-label study in unmethylated MGMT GBM. IV injection of autologous CD34+ HSPCs genetically modified to deliver human interferon-α2 (Temferon) specifically target the tumor with Tie-2 expressing macrophages. The study aims to evaluate the short-term (up to 90 days) and long-term (up to 2 years) tolerability and safety of five escalating doses of Temferon in up to 27 GBM patients.

Results

As of 7th May 2024, 23 GBM patients in 8 cohorts received incremental doses of Temferon up to 4 million cells/kg and 5 patients were still alive after infusion, with a mOS of 17 months (95% CI), with 30% of patients surviving up to 2 years and a mPFS of 8.3 months following initial surgery. To date, no DLTs have been identified. In all patients, rapid engraftment of modified cells and fast hematological recovery have been observed (<=18 days). SAEs were attributed to conditioning chemotherapy required for autologous stem cell transplantation or disease progression (GBM). One SUSAR has occurred (GGT elevation). Successful Temferon engraftment occurred with progeny identified up to 3 years after infusion. Very low IFNα plasma concentrations were detected, indicating a tight regulation of vector expression. In seven patients underwent second surgery, engineered cells (6 out of 7) were detected within the bulk tumor lesion or CD45+ isolated cells (range 1-6%). Local IFNa release inside the tumor was achieved as shown by upregulation of IFN response gene signature and IFNa detection in CSF, often anticipating/concomitant to GBM progression. One stable lesion appeared to be associated with the presence of an IFN high, M1-type myeloid compartment and cytotoxic T cell clones in the TME.

Conclusions

These data corroborate the initial evidence on the safety and tolerability of Temferon and the potential to reprogram GBM TME and elicit T cell-mediated immune responses.

Clinical trial identification

NCT03866109.

Legal entity responsible for the study

Genenta Science Spa.

Funding

Genenta Science Spa.

Disclosure

F. Ciceri: Non-Financial Interests, Institutional, Principal Investigator: Genenta Science Spa. B. Gentner: Financial Interests, Personal, Stocks/Shares: Genenta Science Spa; Financial Interests, Personal, Financially compensated role: Genenta Science Spa; Financial Interests, Personal, Research Funding: Genenta Science Spa; Financial Interests, Personal, Advisory Role: Genenta Science Spa. M. Eoli: Non-Financial Interests, Institutional, Principal Investigator: Genenta Science Spa. A. Capotondo: Non-Financial Interests, Personal, Full or part-time Employment: Genenta Science Spa. S. Mazzoleni: Non-Financial Interests, Personal, Stocks/Shares: Genenta Science Spa; Financial Interests, Personal, Full or part-time Employment: Genenta Science Spa. L. Naldini: Financial Interests, Personal, Stocks/Shares: Genenta Science Spa; Financial Interests, Personal, Financially compensated role: Genenta Science Spa; Financial Interests, Personal, Advisory Role: Genenta Science Spa; Financial Interests, Personal, Research Funding: Genenta Science Spa. C. Russo: Financial Interests, Personal, Full or part-time Employment: Genenta Science Spa; Non-Financial Interests, Personal, Stocks/Shares: Genenta Science Spa. G. Finocchiaro: Financial Interests, Institutional, Coordinating PI: Genenta Science Spa. All other authors have declared no conflicts of interest.

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