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Opinion Article

New Treatments for Synovial Cell Sarcoma with Genetically Modified T-Cell?

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Synovial cell sarcoma is rare but very aggressive tumour if not treated early, due to the painless nature of this tumour patients normally come in late and advances stage, can occur in bones, muscle cells, cartilages, ligaments and de-novo from pleuripotent stem cells from asnywhere in the body but most commonly arm, leg, or foot, and near joints such as the wrist or ankle and possibly from any joints in the body, even from soft tissues of lung and abdomen, the other name for this tumour is called malignant synovioma.The 5 year survival after the effective primary treatment is 30-75% and the survival rate is less than 5% if the tumour recurred within 1 year of primary treatment and that's why new treatments are explored continuously. Due to late recognition and diagnosis of this rare tumour leads to many problems in treatment and in disease course. This tumour can occur at any age but is most common in growing periods like teen agers and adolescents. This tumour can spread to any organ in the body but most commonly distant metastases occur in lungs. Synovial sarcomas actually a misnomer as previously thought, now with advances in cell structure advances, these tumours can occur not only from synovial cells but from any cell of bone, muscle, tendon, ligaments and cartilage forming cells and supporting cells. These tumours occur with equal propensity in both men and women of younger age. If diagnosed early and treated early with surgery alone patients can be cured completely without any morbidity and mortality [1].

In a recently published phase 2 clinical trial 40%of advanced synovial cell sarcomas shown good response after single injection of afamitresgene autoleucel, a modified T cell infusion. This may me the future best treatment for these types of tumours and possibly other tumours as well. The durability of response is still under investigation and the early results ready to be presented in the upcoming ASCO meeting.

As we all know these synovial cell,myxoid and round sarcomas(MRCLS) are very aggressive and have propensity to recur both locally and systemically with available effective therapies.IHC over these tumours shown that above mentioned tumours over express the MAGE A4,a melanoma associated antigen 4.This new treatment mentioned above is a genetically modified autologous melanoma associated antigen 4 specificTcelltherapy.

Afamitresgene autoleucel comprised of autologous cells collected by leukapheresis, this is processed to isolate CD4 and CD8 cells.by using lenti-viral vector, these T cells are genetically altered to express a MAGE-A4–specific T-cell receptor, and These MAGE-A4 antigens are highly expressed in many tumours, which could suggest broad spectrum applicability in multiple cancer therapies. After modification, these cells are expanded using CD3/CD28 beads and followed by cryopreservation for stabilisation and maturation of modified cells before being the administration of this to the needy patients who underwent a lympho-depleting treatment.

With data from phase 1 ADP-A2M4 trial showed that 44% (n = 7/16) patients with synovial sarcoma achieved a partial response (PR) as per RECIST criteria, 94% of patients (n = 15/16) experiencing good disease control, median duration of response was 28 weeks, 2 PRs beyond 72 weeks at the time of data presentation, 11/16 patients were alive, the median overall survival (OS) had not yet been reached.

The phase 2 trial conducted after phase 1 results done to examine the efficacy, safety, and tolerability of Afamitresgene autoleucel in patients with synovial sarcoma and MRCLS,This treatment targets MAGE A4 antigens. The trial mentioned above included 15-75 aged patients of synovial sarcoma and HLA2 positive with MAGE A4 over expression in at least 30%of cells. All these patients had received 1st line chemotherapy with Anthracycline or Ifosfamide based chemotherapies, then undergo leukopheresis for T cells and these extracted T cells reengineered and genetically modified outside the body, once ready this genetically modified bag of blood to be reinfused to the same patient. Of the 37 patients received this therapy, 32 are synovial sarcoma, 5 are myxoid-round cells sarcoma, the overall response rate (ORR) was 39%. this treatment was well tolerarated with minimal, and manageable side effects [2]. The ORR achieved with the this agent was slightly higher in patients with synovial sarcoma (n = 12/29), at 41.4% and in patients with MRCLS,

the ORR with afami-cel was 25.0% (n = 1/4). Objective responses observed across a wide range of cell doses and MAGE-A4 antigen expression levels, the responses achieved with the agent appear to be more durable, with a median DOR that has not yet been reached.

Afamitresgene autoleucel treatment was determined to have a favourable safety profile, most treatment related adverse effects be consistent with those typically experienced by patients with cancer who are receiving chemotherapy and immunotherapy.About 95% of patients experienced any-grade adverse events, 92% had toxicities that were grade 3 and higher. Few of the adverse effects experienced with the agent and were decreased lymphocyte count (84%, any grade; 84% grade 3 or higher), decreased neutrophil count (73%; 68%), decreased white blood cell count (68%; 62%), cytokine release syndrome (59%; 3%), and decreased platelet count (27%; 16%).

Phase 3 trial result waited in the near future.

Along with doxorubicin and Ifosfamide based treatments, the newer treatments available are tyrosine kinase inhibitors, epigenetic modulators, molecules interfering with DNA damage response, and immunotherapeutic drugs and combination of these molecules have produced excellent responses [3, 4].

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