National Institute for Health Research

NIHR Innovation Observatory
Evidence Briefing: May 2017

NY-ESO-1 T cells for the treatment of synovial sarcoma

NIHR (HSRIC) ID: 12402 NICE ID: 9408

LAY SUMMARY

Sarcomas are rare cancers developing in the muscle, bone, nerves, cartilage, tendons, blood vessels and the fatty and fibrous tissues. They can affect almost any part of the body. Three types of sarcoma mainly occur, including soft tissue sarcoma. Synovial sarcoma is one of the most common form hereby. It develops in cells and around joints and tendons. It occurs throughout the body, but often near the knee. Symptoms include a lump or swelling in the soft tissue of the body or under the skin. The earlier sarcoma is diagnosed the better the chances of successful treatment. Soft tissue sarcomas account for less than 1% of cancers in the UK.

NY-ESO-1 T cells are genetically modified T cells that are re-infused into the patient. It is being developed for the treatment of cancers including melanoma, multiple myeloma and synovial sarcoma. It is currently in Phase III clinical trials.

TARGET GROUP

Synovial sarcoma

TECHNOLOGY

DESCRIPTION

NY-ESO-1 T cells [3377794; anti-NY ESO1 TCR PBL, GSK-3377794, NY-ESO SPEAR, Adaptimmune; NY-ESO1 (c259) TCR Tcells] is a treatment for cancer in patients with the HLA-A2 or HLA-A1 tissue-type markers. The therapy is based on SPEAR T-cell (Specific Peptide Enhanced Affinity Receptor T-cells). Autologous T cells are genetically engineered to express an affinity-enhanced T cell receptor (TCR) that is specific for a peptide NY-ESO-1 cancer antigen (referred to as NY-ESO SPEAR T-cell therapy). The genetically modified T cells are then re-infused into the patient.[1] It is being developed by Adaptimmune for the treatment of cancers including melanoma, multiple myeloma and synovial sarcoma. It is also under development for the treatment of liposarcoma.[2]

In the Phase III clinical trial for soft tissue sarcoma patients receive NY-ESO-1 with modified CTX/flu (CTX 600mg/m^2/fludarabine 30mg/m^2) X 3 days.[3]

INNOVATION and/or ADVANTAGES

If licenced, NY-ESO-1 T cells will offer an additional treatment option for patients with synovial sarcoma.

DEVELOPER

Adaptimmune

AVAILABILITY, LAUNCH or MARKETING

NY-ESO-1 T cells received an Orphan Drug Status in the EU for soft tissue sarcoma. It further received breakthrough therapy designation for inoperable or metastatic synovial sarcoma in the USA and PRIME status in the EU.[2]

It is currently in clinical trials phase III.[1]

PATIENT GROUP

BACKGROUND

Sarcomas are rare cancers that develop in the muscle, bone, nerves, cartilage, tendons, blood vessels, and fatty and fibrous tissues. They can affect almost any part of the body and three types exist: soft tissue sarcoma, bone sarcoma and gastrointestinal stromal tumours.[4] Soft tissue sarcomas develop in supporting or connective tissue,[5] and one of the most common types is synovial sarcoma. It develops in cells around joints and tendons but is typically found near the knee. Symptoms include a lump or swelling in the soft tissue of the body or under the skin, and the earlier the diagnosis the better the chances of successful treatment.[6]

Synovial sarcoma appears to arise from as yet unknown multipotent stem cells that are capable of differentiating into mesenchymal and/or epithelial structures and lack synovial differentiation. Like other soft tissue sarcomas, synovial sarcoma is difficult to recognise purely on the basis of histological appearance. These tumours can be identified only by immunohistochemical analysis, ultrastructural findings and demonstration of the specific chromosomal translocation.[8]

Five-year survival rate is estimated to be between 50% and 60% for soft tissue sarcomas, however, this is dependent on various characteristics such as patient age, size of tumour, its depth and histopathological grade.[5]

CLINICAL NEED and BURDEN OF DISEASE

Collectively, bone and soft tissue sarcomas account for around 1% of all malignancies in the UK. Figures show that there were 3298 new diagnoses of soft tissue sarcoma during 2010 in the UK.[7]. Approximately half of all soft tissue sarcoma patients with intermediate or high-grade tumours develop metastatic disease requiring systematic treatment. Furthermore, sarcomas constitute a heterogeneous group of tumours of mesenchymal cell origin, often with a distinct age distribution, site of presentation, natural biological behaviour and prognosis. The heterogeneity of this kind of tumour affects the incidence number, which has generally been under-reported.[8]

Although soft tissue sarcomas may occur at any age, patients tend to be younger than the majority of cancer patients. 16% of bone or soft tissue sarcomas are diagnosed in patients less than thirty years of age, compared to around 2% of all cancers. 37% of bone or soft tissue sarcoma patients are aged less than 50 years. Sarcomas make up 15% of all childhood cancers (0 to 14 years) and 11% of all cancer diagnoses in teenagers and young people (15 to 24 years).[4]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology appraisal in development. Olaratumab in combination with doxorubicin for treating advanced soft tissue sarcoma [ID595]. Expected TBC.
- NICE Technology appraisal. Trabectedin for the treatment of advanced soft tissue sarcoma [TA185]. February 2010.
- NICE quality standard. Sarcoma [QS78]. January 2015.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Cancer: Soft Tissue Sarcoma (Adult). B12/S/a

OTHER GUIDANCE

No other guidance was identified.

CURRENT TREATMENT OPTIONS

Treatment of synovial sarcoma depends on the stage and grade of the cancer. The most common treatment option is surgery, therefore an area of normal tissue, known as the margin, is required in order for the tumour to be removed. In the case that limbs are affected, patients will receive limb-sparing surgery whereby, the affected bone is removed and replaced with a specially designed metal replacement. If nerves and bloods vessels around the bone are affected, partial amputation is required.

An alternative treatment option is radiotherapy which involves high-energy radiation used either before or after surgery to destroy cancer cells. Chemotherapy is another treatment for synovial sarcoma.[6] Adjuvant doxorubicin- and cyclophosphamide-based chemotherapies are recommended as well as combinations of doxorubicin and bolus ifosfamide. Some studies showed promising results in the treatment of synovial cell sarcoma xenografts with a murine monoclonal antibody. An additional innovative technique being developed is a SYT-SSX-derived peptide vaccine.[9]

EFFICACY and SAFETY

Trial	NCT01343043
Sponsor	Adaptimmune
Status	Ongoing
Source of Information	Trial registry[11]
Location	EU (incl UK), Canada, France, USA
Design	Non-randomized, parallel assignment, no masking, treatment
Participants	Estimated N= 65, aged >4; synovial carcinoma that has been treated with standard chemotherapy containing ifosfamide and/or doxorubicin and remains: unresectable or metastatic or progressive/persistent or recurrent disease. Measurable disease.
Schedule	Experimental: Cohort 1 treated with NY-ESO-1 T Cells High NY-ESO-1 expression and the use of cyclophosphamide plus fludarabine. (COMPLETE). Then cytoreductive chemotherapy followed by infusion with NY-ESO-1(c259) transduced autologous T cells. Subjects will receive one infusion of NY-ESO-1 genetically engineered T cells on Day 0. Experimental: Cohort 2 treated with NY-ESO-1 T Cells Low NY-ESO-1 expression and the use of cyclophosphamide plus fludarabine. Then cytoreductive chemotherapy followed by infusion with NY-ESO-1(c259) transduced autologous T cells. Subjects will receive one infusion of NY-ESO-1 genetically engineered T cells on Day 0. Experimental: Cohort 3 treated with NY-ESO-1 T Cells High NYESO-1 expression and the use of cyclophosphamide only for lymphodepletion rather than fludarabine. (COMPLETE) Then cytoreductive chemotherapy followed by infusion with NY-ESO-1(c259) transduced autologous T cells. Subjects will receive one infusion of NY-ESO-1 genetically engineered T cells on Day 0. Experimental: Cohort 4 treated with NY-ESO-1 T Cells

	High NY-ESO-1 expression and the use of reduced dose cyclophosphamide plus fludarabine regimen. Then cytoreductive chemotherapy followed by infusion with NY-ESO-1(c259) transduced autologous T cells. Subjects will receive one infusion of NY-ESO-1 genetically engineered T cells on Day 0.
Follow-up	Not reported.
Primary Outcomes	• Proportion of subjects with a confirmed Complete Response (CR) or Partial Response (PR) in each cohort [Time Frame: 1 Year] • Evaluation of efficacy and duration of response of the treatment by assessment of Best Overall Response Rate according to RECIST v1.1
Secondary Outcomes	• Number of subjects with dose-limiting toxicity (DLT) and adverse events (AE), including serious adverse events. • Evaluation of the persistence of genetically modified T cells. Percentage of total gene modified T cells with memory subtype. • After progressing and after receiving a 2nd dose of NY-ESO-1^{c259}T, proportion of subjects with a confirmed Complete Response.
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated primary completion date October 2017. Estimated study completion date March 2028.

ESTIMATED COST and IMPACT

COST

The cost of NY-ESO-1 is not known yet.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS and CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☒ Other: *improved patient convenience, wider societal benefits*

☐ No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☐ Decreased use of existing services

☐ Re-organisation of existing services

☐ Need for new services

☐ Other.

☒ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☐ Increased drug treatment costs

☐ Reduced drug treatment costs

☐ Other increase in costs

☐ Other reduction in costs:

☐ Other

☒ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

INFORMATION FROM

Adaptimmune did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHRIO has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

REFERENCES

1 AdisInsight. *NY-ESO-1 T cells.* Available from: http://adisinsight.springer.com/drugs/800038362 [Accessed 09th May 2017].

2 Pharmaprojects. *NY-ESO-1 T cells*.

3 Trialtrove. *A pivotal study of NY-ESO-1 in patients with Synovial Sarcoma including Myxoid Round Cell Liposarcoma*.

4 Sarcoma UK. *Understanding Sarcoma*. Available from: https://sarcoma.org.uk/about-sarcoma/understanding-sarcoma-0 [Accessed 09th May 2017].

5 Sarcoma UK. *Soft tissue sarcoma*. Available from: https://sarcoma.org.uk/sarcoma-types/soft-tissue-sarcoma [Accessed 09th May 2017].

6 Sarcoma UK. *Synovial sarcoma*. Available from: https://sarcoma.org.uk/sarcoma-types/synovial-sarcoma [Accessed 09th May 2017].

7 NICE 2015. *Quality Standard (QS78)*. Available from: https://www.nice.org.uk/guidance/qs78/chapter/Introduction [Accessed 09th May 2017].

8 Ruggiero A, 2004. *Synovial sarcoma*. Available from: https://www.orpha.net/data/patho/GB/uk-synovialsarcoma.pdf [Accessed 09th May 2017].

9 Dangoor A, Seddon B, Gerrand C, Grimer R, Judson JW. *UK guidelines for the management of soft tissue sarcomas*. 2016 Available from: https://clinicalsarcomaresearch.biomedcentral.com/articles/10.1186/s13569-016-0060-4 [Accessed 09 May 2017].

10 Vargas B. *Synovial Cell Sarcoma Treatment & Management*. 2016 Available from: http://emedicine.medscape.com/article/1257131-treatment#d9 [Accessed 09th May 2017].

11 ClinicalTrials.gov. *A Pilot Study of Genetically Engineered NY-ESO-1 Specific NY-ESO-1^{c259}T in HLA-A2+ Patients With Synovial Sarcoma* (NY-ESO-1). Available from: https://clinicaltrials.gov/ct2/show/NCT01343043 [Accessed 18.05.2017].