A Pilot Trial Using Lymphocytes Genetically Engineered with an NY-ESO-1-Reactive T-cell Receptor: Long-term Follow-up and Correlates with Response

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Abstract

Purpose: Although adoptive cell therapy can be highly effective for the treatment of patients with melanoma, the application of this approach to the treatment of other solid tumors has been limited. The observation that the cancer germline (CG) antigen NY-ESO-1 is expressed in 70% to 80% and in approximately 25% of patients with synovial cell sarcoma and melanoma, respectively, prompted us to perform this first-in-man clinical trial using the adoptive transfer of autologous peripheral blood mononuclear cells that were retrovirally transduced with an NY-ESO-1-reactive T-cell receptor (TCR) to heavily pretreated patients bearing these metastatic cancers.

Experimental Design: HLA-0201 patients with metastatic synovial cell sarcoma or melanoma refractory to standard treatments and whose cancers expressed NY-ESO-1 received autologous TILs following a lymphodepleting preparative chemotherapy. Response rates using Response Evaluation Criteria in Solid Tumors (RECIST), as well as immunologic correlates of response, are presented in this report.

Results: Eleven of 18 patients with NY-ESO-1+ synovial cell sarcomas (61%) and 11 of 20 patients with NY-ESO-1+ melanomas (55%) who received autologous T cells transduced with an NY-ESO-1-reactive TCR demonstrated objective clinical responses. The estimated overall 3- and 5-year survival rates for patients with synovial cell sarcoma were 38% and 14%, respectively, whereas the corresponding estimated survival rates for patients with melanoma were both 33%.

Conclusions: The adoptive transfer of autologous T cells transduced with a retrovirus encoding a TCR against an HLA-A0201 restricted NY-ESO-1 epitope can be an effective therapy for some patients bearing synovial cell sarcomas and melanomas that are refractory to other treatments. Clin Cancer Res; 21(5); 1019–27. ©2014 AACR.

Introduction

The in vitro expansion of tumor-infiltrating lymphocytes (TIL) from fresh melanoma samples frequently leads to the generation of T cells reactive with autologous tumor cells. The administration of these TILs following lymphodepleting chemotherapy can mediate objective tumor regressions in 50% to 70% of patients with metastatic melanoma, with some patients achieving durable complete regressions (1). Although there is evidence that T cells derived from additional tumor types can recognize autologous tumors (2–4), tumor-reactive TILs are less frequently obtained from other tumors. One strategy for addressing the difficulty in generating tumor-reactive T cells is the genetic modification of autologous T cells to express cloned T-cell receptors (TCR) directed against shared tumor antigens. Cancer germline (CG) antigens, molecules expressed in a wide variety of tumor types but often not expressed in any adult tissues with the exception of germline cells that lack HLA class I and II expression, represent attractive targets for these therapies (5). The CG antigen NY-ESO-1 is expressed in 10% to 50% of metastatic melanomas, lung, breast, prostate, thyroid, and ovarian cancers (6–9) as well as between 70% and 80% of synovial cell sarcomas (10). In 2011, we reported preliminary results of this first-in-man clinical trial utilizing the adoptive transfer of autologous peripheral blood mononuclear cells (PBMC) that were transduced with a high-affinity TCR directed against an HLA-A0201–restricted NY-ESO-1 epitope to 6 and 11 patients with metastatic synovial cell sarcoma and metastatic melanoma, respectively (11). In the current study, we present clinical response data for 12 additional synovial cell sarcoma patients and 9 additional patients with melanoma enrolled in this trial, updated response data for the 17 patients characterized in the first report, and analyses of the in vitro antitumor reactivity and in vivo persistence following adoptive transfer of the administered T cells.

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Note: Supplementary data for this article are available at Clinical Cancer Research Online (http://clincancerres.aacrjournals.org/).

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Patients and clinical trial design

Patients 18 years or older expressing HLA-A*0201 with either metastatic synovial cell sarcoma or metastatic melanoma refractory to standard chemotherapy and whose tumors expressed NY-ESO-1 as determined by IHC staining were enrolled in the current trial. All patients’ tumors stained strongly (2–4+ intensity in greater than 50% of cells) for NY-ESO-1 antigen expression using the specific anti-NY-ESO-1 monoclonal antibody E978 (ref. 12; Invitrogen).

Patients 7–9 (first treatment), as well as 5, 6, 24, and 27 (second treatment), were immunized with a recombinant AVIPOX virus encoding the NY-ESO-1 T-cell epitope (AVIPOX-ESO) at the time of adoptive transfer as well as 2 weeks following transfer. There was no apparent immunologic or clinical impact of this vaccination and thus all patients with synovial cell sarcoma or melanoma in this study are considered as individual cohorts.

This clinical trial (NCT00670748) was conducted in the Surgery Board, the NIH Office of Biotechnology Activities, and the FDA Institutional Biosafety Committee, the NCI Institutional Review Board, the NIH Of melanoma had often received multiple treatments including IL2, multiple chemotherapy regimens, and patients with metastatic melanoma, including 11 patients also described in the previous report, and 20 HLA-A*0201 patients with NY-ESO-1+ metastatic melanoma, including 11 patients also described in the previous report (11), received nonmyeloablative chemotherapy followed by a median of 5.5 × 10^8 T cells transduced with an anti-NY-ESO-1 TCR (range 0.9–13 × 10^8) plus systemic IL2. Characteristics of the patients and of the administered cells are shown in Table 1. With the exception of patients 4 and 17, more than 50% of the administered T cells were CD8+, and a median of 78% and 62% of the administered CD8+ and CD4+ T cells, respectively, bound to a tetramer prepared with HLA-A*0201 and the NY-ESO-1:157-165 peptide (Beckman Coulter), as previously indicated (11).

Evaluation of IFNγ secretion, IFNγ ELISpot responses

Cocultures of in vitro cultured T cells and PBMC were carried out with target cells for 18 hours and secreted IFNγ detected in a standard ELISA assay (14). ELISpot assays were carried out by incubating TIL or PBMC overnight in the absence of exogenous cytokine and then cocultured with target cells for 18 hours, after which the number of IFNγ-secreting T cells were enumerated, as previously described (15).

Results

Patient and treatment characteristics

A total of 18 HLA-A*0201+ patients with NY-ESO-1+ metastatic synovial cell sarcomas including 6 patients described in a previous report, and 20 HLA-A*0201+ patients with NY-ESO-1+ metastatic melanoma, including 11 patients also described in the previous report (11), received nonmyeloablative chemotherapy followed by a median of 5.5 × 10^8 T cells transduced with an anti-NY-ESO-1 TCR (range 0.9–13 × 10^8) plus systemic IL2. Characteristics of the patients and of the administered cells are shown in Table 1. With the exception of patients 4 and 17, more than 50% of the administered T cells were CD8+, and a median of 78% and 62% of the administered CD8+ and CD4+ T cells, respectively, bound to a tetramer prepared with HLA-A*0201 and the NY-ESO-1:157-165 peptide.

All of the patients with synovial cell sarcoma on the trial had progressive metastatic disease following extensive pretreatment consisting of surgery, often in combination with radiation and multiple chemotherapy regimens, and patients with metastatic melanoma had often received multiple treatments including IL2, radiation therapy, IFNα, or GM-CSF (11).

Clinical results

Eleven of the 18 patients with synovial cell sarcoma (61%) who received autologous TCR-transduced T cells experienced objective responses by RECIST (Response Evaluation Criteria in Solid Tumors) criteria (Tables 2 and 3). Responses to a first treatment with the 1G4-ε95:LY TCR are shown with the exception of patient 2, who exhibited a partial response lasting 6 months to an initial infusion of TCR-transduced T cells, as well as a partial response lasting 9 months following a second infusion of a similar T-cell product, for a total combined response of 18 months following
the initial treatment (Table 2). Five additional patients (1, 3, 5, 6, 8), received but failed to respond to a second infusion of 1G4-αLY-transduced T cells, and patient 2 received but failed to respond to a third treatment with transduced T cells.

Two patients with synovial cell sarcoma have ongoing clinical responses: patient 7, who exhibited a nearly complete regression of multiple lung metastases, as well as substantial regression of a large pelvic bony lesion, both sustained nearly 4 years following treatment (Fig. 1A), and patient 15, who demonstrated a complete regression of all metastatic lesions, including multiple lung metastases maintained more than a year following treatment (Fig. 1B). Partial responses lasted from 3 months to 18 months, and the estimated overall 3- and 5-year survival rates for patients with synovial cell sarcoma were 38% and 14%, respectively (Fig. 2A).

Eleven of the 20 patients with melanoma (55%) experienced objective responses to a first treatment with 1G4-αLY TCR-transduced T cells. Two patients (24 and 27) failed to respond to a second infusion of 1G4-αLY-transduced T cells. Four patients with melanoma had complete responses, three ongoing at 40 to 58 months following treatment. One of the complete responders, patient 29, exhibited regression of multiple liver and lung metastases (Fig. 1C and D). Partial responses lasting 3 to 28 months were seen in 7 patients with melanoma (Tables 2 and 3) including patient 37, who was exhibiting an ongoing partial response 6 months after adoptive transfer, when he was censored because of the development of a second unrelated cancer. The estimated overall 3- and 5-year survival rates for patients with melanoma were both 33% (Fig. 2B).

All patients experienced the transient neutropenia and thrombocytopenia induced by the preparative regimen and the transient toxicities associated with IL2. Hematologic and chemical values returned to baseline in all but one patient who was the single treatment-related death in this protocol. This patient, a 40-year-old male (patient 12), developed septic shock from an Escherichia coli bacteremia while he was neutropenic and died 3 days following adoptive T-cell transfer. No toxicities

<table>
<thead>
<tr>
<th>Table 1. Characteristics of patients and administered T cells</th>
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<tbody>
<tr>
<td><strong>Patient</strong></td>
</tr>
<tr>
<td>Synovial cell sarcoma</td>
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<tr>
<td>1</td>
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<td>2</td>
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<td>3</td>
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<td>16</td>
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<td>38</td>
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Abbreviations: ln, lymph node; sc, subcutaneous; lu, lung; bo, bone; panc, pancreas; sb, small bowel; ki, kidney; br, brain; spl, spleen; pl, pleura; hi, hilum; S, surgery; R, radiation; I, immunotherapy; C, chemotherapy.

The number of chemotherapy regimens administered to synovial cell sarcoma patients before adoptive transfer is noted in parentheses.

The T cells administered to patient 12, who developed sepsis and died 3 days following adoptive transfer, were not further characterized.
were attributed to the transferred cells, in accord with the lack of expression of NY-ESO-1 on normal tissues with the exception of germline cells that do not express MHC molecules and thus are immunologically inert.

Clinical responses were observed in 4 of the 5 patients with synovial cell sarcoma who were also vaccinated with the recombinant AVIPOX-ESO virus, one of which only lasted for 3 months, and in 2 of the 6 vaccinated melanoma patients (Table 2). These response rates did not appear to be significantly different from patients who did not receive the vaccine, but the small number of patients receiving this treatment made it impossible to draw any conclusions about the effect of immunization on clinical response to therapy with NY-ESO-1 TCR-transduced cells.

Table 3. Clinical response to adoptive transfer of T cells transduced with anti-NY-ESO-1 TCR

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Total</th>
<th>PR (n)</th>
<th>CR (n)</th>
<th>OR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial cell sarcoma</td>
<td>18</td>
<td>10 (55)</td>
<td>7 (39)</td>
<td>1 (6)</td>
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<tr>
<td></td>
<td></td>
<td>47, 18, 11, 10, 8, 7, 5, 4, 3, 3</td>
<td></td>
<td>11 (61)</td>
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<tr>
<td>Melanoma</td>
<td>20</td>
<td></td>
<td></td>
<td>4 (20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>28, 10, 8, 6+, 5, 3, 3</td>
<td>58+, 54+, 40+, 24</td>
<td>11 (55)</td>
</tr>
</tbody>
</table>

NOTE: Response data updated as of December 1, 2014, or the last follow-up date. Abbreviations: PR, partial response; CR, complete response; OR, objective response.
Immunologic correlates of response

Attempts were then made to identify factors that are associated with response to therapy mediated by the NY-ESO-1 TCR. There was no significant difference between the number of T cells administered to patients with synovial cell sarcoma and melanoma (Fig. 3A) or between the IFNγ ELISPOT responses of T cells from patients with synovial cell sarcoma and melanoma to either NY-ESO-1 peptide pulsed target cells (Fig. 3B) or an HLA-A*0201+ and NY-ESO-1+ melanoma cell line (Fig. 3C). Given these findings and the relatively small number of patients in each cohort, we attempted to identify factors that are associated with response to therapy combining both patients with synovial cell sarcoma and melanoma. The results indicated that clinical responses were associated with higher numbers of administered T cells (P < 0.02; Fig. 3D) and higher numbers of IFNγ ELISPOTs following stimulation with NY-ESO-1 peptide pulsed target cells (P < 0.02; Fig. 3E), but not an HLA-A*02:01+ and NY-ESO-1+ tumor cell line (Fig. 3F).

The percentages of CD8+ and NY-ESO-1 tetramer+ T cells in the peripheral blood of patients approximately one month following transfer were highly variable, ranging between less than 1% and 72% of CD3+ T cells, whereas the percentage of CD4+ and NY-ESO-1 tetramer+ T cells ranged between less than 1% and 49% of CD3+ T cells (Table 2). The median percentage of CD8+ NY-ESO-1 tetramer+ T cells detected in the peripheral blood of responders and nonresponders at this time was 11% and 8.5%, respectively, whereas the median percentage of CD4+ NY-ESO-1 tetramer+ T cells at this time was 8% and 6.5%, respectively. Clinical responses were not associated with persistence at one month of CD8+ (Supplementary Fig. S1A) or CD4+ (Supplementary Fig. S1B) NY-ESO-1 tetramer+ T cells, results consistent with those seen in the prior study evaluating responses in a subset of these patients (11). One month following adoptive transfer, PBMC isolated from responders and nonresponders generated a median of 1,650 and 973 IFNγ ELISPOTs per 10^5 cells in response to HLA-A*0201+ target cells pulsed with the NY-ESO-1:157-165 peptide (Supplementary Fig. S1C), and a median of 27 and 62 IFNγ ELISPOTs per 10^5 cells in response to HLA-A*0201+ and NY-ESO-1+ tumor cells, respectively (Supplementary Fig. S1D), but these differences were not statistically significant. In addition, immunization with recombinant NY-ESO-1 AVIPOX did not significantly impact either the persistence of CD8+ or CD4+ T cells reactive with the NY-ESO-1 tetramer in peripheral blood approximately one month following adoptive transfer (Supplementary Fig. S2A and S2B) or IFNγ ELISPOT responses of peripheral T cells to either HLA-A*02:01+ cells pulsed with the NY-ESO-1 peptide or an HLA-A*02:01+ and NY-ESO-1+ tumor cell line (Supplementary Fig. S2C and S2D).

Discussion

The durable complete cancer regressions observed using cell transfer immunotherapy for melanoma in multiple clinical trials (1, 13, 16) have stimulated efforts to genetically modify lymphocytes to improve their antitumor efficacy and to extend the range of tumors types that can be treated. In the first reported trial to examine the in vivo efficacy of TCR-transduced T cells in patients with cancer, the adoptive transfer of autologous T cells that were transduced with a MART-1-reactive TCR lead to tumor regression in 2 of 13 treated patients (17). In subsequent trials carried out with higher avidity TCRs, objective clinical responses were seen in 6 of 20 (30%) patients treated with autologous T cells that were transduced with a MART-1-reactive TCR (17) and in 3 of 16 (19%) patients treated with a gp100-reactive TCR (15). Severe normal tissue toxicities resulting from expression of these antigens in normal melanocytes present in the skin, eye, and ear were observed in these trials, emphasizing the need to target protein such as CG antigens that are not expressed in essential normal tissues.

The NY-ESO-1 protein represents a CG antigen expressed in between 70% and 80% of synovial cell sarcomas (10) and in 10% to 50% of a variety of more common malignancies that include melanoma, bladder, lung, breast, and ovarian cancer (6, 7, 9), but not in adult normal tissues except for testes, which does not express HLA class I molecules and is thus immunologically unrecognizable.
protected. The adoptive transfer of an in vitro sensitized autologous CD4⁺ T-cell clone that recognized an HLA-DP 04 restricted NY-ESO-1 peptide mediated regression of metastatic melanoma in 1 of 9 patients (16, 18). In 2010, we presented preliminary results of the first adoptive cellular immunotherapy trial for solid cancers to utilize the transfer of autologous PBMC transduced with a CG-reactive TCR. In that study as well as the current one, patients received autologous PBMCs that were transduced with a TCR, termed 1G4-αLY, that possessed a high avidity for the HLA-A*0201-restricted NY-ESO-1:157-165 epitope (11). Response rates of 45% and 67% were observed in the initial cohorts of melanoma and synovial cell sarcoma patients, respectively, all of whom had progressive disease after extensive prior treatment. Clinical responses to therapy were not associated with the persistence of adoptively transferred T cells, as determined either using NY-ESO-1 tetramer binding or antigen-specific ELISPOT to evaluate TCRs, although only 6 patients with synovial sarcoma, as well as 11 patients with melanoma, were evaluated in the previous study. The current study was carried out on 18 patients with synovial cell sarcoma and 20 patients with melanoma, including
the 6 patients with synovial cell sarcoma and 11 patients with melanoma analyzed in the previous study. Objective responses were observed in 11 of the 18 patients (61%) with synovial cell sarcoma and 11 of the 20 patients with melanoma (55%) who received autologous TCR-transduced cells. The nonmyeloablative chemotherapy regimen administered to all of the patients in this trial may have contributed to the transient partial responses lasting from 3 to 11 months seen in 8 of the patients with synovial cell sarcoma, and lasting from 3 to 10 months in 5 of the treated patients with melanoma. The 18 patients with synovial cell sarcoma evaluated in the current trial, however, had progressed after receiving multiple rounds of chemotherapy. Thus, it is unlikely that the preparative chemotherapy regimen was responsible for the complete response seen in one of the patients with synovial sarcoma that is ongoing at one year, and the substantial partial response seen in another patient who was treated with auto TCR-transduced cells. As noted previously, the persistence of anti-NY-ESO-1 TCR-transduced T cells in peripheral blood approximately one month following transfer was not associated with response to therapy (11). This contrasts with observations in our trial involving treatment with MART-1 and gp100 TCR-transduced T cells indicating that response to therapy was associated with the levels of persistent peptide reactive and tumor-reactive T cells (15). It is difficult to draw general conclusions as to the relationship between the persistence or antitumor activity of the TCR-transduced T cells and response to therapy, however, given the relatively small numbers of patients treated in these trials.

The objective response rates observed in previous clinical trials involving immunization with peptides derived from tumor antigens, whole proteins, as well as recombinant viral constructs encoding tumor antigens were generally 5% or lower [reviewed in ref. (20)]. Nevertheless, in an attempt to determine the effects of tumor antigen vaccination on responses to adoptively transferred T cells, 11 of the 38 patients treated in the current trial were immunized with a recombinant NY-ESO-1 AVIPOX vaccine. There was no significant difference, however, between clinical response rates in patients who either did or did not receive the NY-ESO-1 vaccine, and neither the persistence nor the function of peripheral NY-ESO-1-reactive T cells differed significantly between these two patient groups. Other factors such as differences between the levels of homeostatic cytokines or the rates of endogenous lymphocyte reconstitution in individual patients

As noted previously, the persistence of anti-NY-ESO-1 TCR-transduced T cells in peripheral blood approximately one month following transfer was not associated with response to therapy (11). This contrasts with observations in our trial involving treatment with MART-1 and gp100 TCR-transduced T cells indicating that response to therapy was associated with the levels of persistent peptide reactive and tumor-reactive T cells (15). It is difficult to draw general conclusions as to the relationship between the persistence or antitumor activity of the TCR-transduced T cells and response to therapy, however, given the relatively small numbers of patients treated in these trials.

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NY-ESO-1 cells, such as the levels of expression of HLA-A factors that may be relevant to recognition of autologous tumor response to therapy with the anti-NY-ESO-1 TCR. A variety of factors that may be relevant to recognition of autologous tumor cells, such as the levels of expression of HLA-A2, NY-ESO-1, and proteins that influence T-cell recognition including adhesion, inhibitory and costimulatory molecules may have influenced in vitro recognition of the allogeneic tumor cell target and led to the discrepancy between peptide and tumor cell recognition. The number of administered T cells had not previously been associated in our studies with response to therapy with either autologous TIL (1) or autologous PBMC transduced with TCRs directed against HLA-A*02:01–restricted epitopes of MART-1 or gp100 (15), although an association between the number of administered TIL and clinical response has been noted by others (21).

The lack of a correlation between responsiveness and persistence seen in the current study was somewhat unexpected, as the persistence of bulk TIL populations was correlated with response to therapy (22); however, the relatively small number of patients who were evaluated may in part have been responsible for the discrepancies between these trials. The presence of persistent T cells in peripheral blood is not sufficient to mediate responses in all patients, as demonstrated by the relatively high levels of persistence observed in some of the nonresponding patients evaluated in this study as well as the pivotal study (22), and additional factors such as downregulation of HLA and other gene products involved with antigen processing may have played a role in the lack of responses observed in these patients. The limited or undetectable levels of persistence of TCR-transduced T cells observed in peripheral blood one month following therapy from 3 of the patients with synovial cell sarcoma, patients 6, 13, and 18, and 2 of the patients with melanoma, patients 21 and 28, may have been associated with the lack of response observed in these individuals. The relatively short durations of the objective responses seen in some patients who demonstrated relatively high levels of persistence at one month could potentially have resulted from a failure of the T cells to persist for longer time periods, but could not be evaluated because of the limited availability of samples at later time points. Finally, persistence in the periphery may not be strictly correlated with persistence in the tumor, but again, could not be evaluated in this study due to lack of tumor samples.

Expression of the NY-ESO-1 antigen is highly restricted to the tumor and not normal tissues; however, this does not appear to be the case for all CG antigens. The MAGEA3 gene product represents one of the most highly prevalent CG antigens and is significantly expressed in between 30% and 50% in a variety of common cancers. In a recent clinical trial, the adoptive transfer of autologous PBMC transduced with a MAGE-A3–reactive TCR resulted in the deaths of 2 patients due to severe neurologic toxicity. The toxicity appeared to result from cross-reactivity of TCR-transduced T cells with a nearly identical epitope from MAGE-A12, a protein that was found to be expressed at low levels in normal brain tissue (23). In addition, the adoptive transfer of autologous PBMC transduced with an HLA-A1 restricted, MAGE-A3–reactive TCR containing four α chain amino acid substitutions that were introduced to enhance antigen recognition resulted in cardiac arrest and the deaths of the first two patients treated on this protocol (24), which were attributed to cross-reactivity of TCR-transduced T cells with an epitope of titin, a protein that is highly expressed in cardiac tissue (25).

Recent trials have demonstrated that intravenous administration of antibodies targeting inhibitory receptors such as CTLA-4 and PD-1 that are expressed on T cells, as well as inhibitory ligands such as PD-L1 that are expressed on a variety of cell types, can be effective at mediating tumor regressions in patients with some cancers. An overall clinical response rate of approximately 10% was observed in patients with melanoma who received an antibody directed against the inhibitory receptor CTLA-4 (26), and objective response rates of 20% to 30% were seen in patients with melanoma, renal, and non–small cell lung cancer treated with BMS-936558, an antibody against the PD-1 checkpoint inhibitor (27). In addition, clinical responses were seen in between 5% and 15% of melanoma, renal, and non–small cell lung cancer patients who received an antibody directed against the PD-1 ligand PD-L1 (28).

In the current study, patient 7 had previously progressed following treatment with IL2 and anti-PD-L1 antibody but demonstrated a partial response to transfer of NY-ESO-1 TCR-transduced T cells. Combinations of checkpoint inhibitors with adoptive immunotherapies represent one strategy that may lead to enhanced antitumor responses, although a series of trials may be needed to determine the optimal dosage of checkpoint inhibitors and the appropriate sequencing of these treatments.

The factors that were responsible for the lack of response and the short duration of responses seen in the majority of patients evaluated in this protocol are unknown. Antigen loss does not appear to be a major contributor to the lack of responsiveness, as high levels of NY-ESO-1 expression were observed in additional tumor biopsies obtained from 6 of the synovial cell sarcoma patients and 2 of the patients with melanoma following their first treatment but prior to their second treatment with anti-NY-ESO-1 TCR-transduced T cells.

Overall, these findings indicate that treatments using TCRs directed against NY-ESO-1 are effective at safely mediating tumor regression in patients with metastatic, refractory synovial cell sarcoma, and melanoma, and indicate that the total number of T cells and the number of antigen-reactive T cells administered to patients in this trial may represent important factors that influence response to therapy. Furthermore, these findings provide support for development of additional trials targeting NY-ESO-1 as well as other CT antigens expressed in common epithelial cancers.

Disclosure of Potential Conflicts of Interest

S.H. Kassim is an employee of Novartis. No potential conflicts of interest were disclosed by the other authors.

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References


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