INTRODUCTION

The binding of PD-L1 to its receptors, programmed death-1 (PD-1) and B7.1 (CD80), on activated T cells can tumor-infiltrating immune cells (IC) in multiple tumor types, including breast cancer. Chemotherapy remains a mainstay of treatment for mTNBC, with no approved targeted treatment in the United Kingdom.

METHODS

A second post-dose biopsy was taken in the serial biopsy cohort ≈ 4 weeks after first dose of atezolizumab. Association of response with PD-L1 TC or IC status was evaluated both TC and IC. Nab-paclitaxel was used in this study instead of solvent-based paclitaxel because it can be administered while nab-paclitaxel (125 mg/m²) is used in this study instead of solvent-based paclitaxel because it can be administered while nab-paclitaxel (125 mg/m²) is used in this study instead of solvent-based paclitaxel because it can be administered

RESULTS

Nab-paclitaxel was administered for ≥ 4 cycles in the absence of disease progression or unacceptable toxicity. In the serial biopsy cohort (n = 24), single-agent nab-paclitaxel was given on days 1 and 8 of cycle 1; and 2 cycles of atezolizumab were given. Of these patients, 12 had disease progression during or following platinum-based chemotherapy in the metastatic setting; 8 had progressive disease during initial exposure to nab-paclitaxel. PD-L1 IC0: < 1% IC expressing PD-L1 PD-L1 TC0: < 1% TC expressing PD-L1.

CONCLUSIONS

Two patients had a decrease in tumor burden after an initial increase or the appearance of new lesions. Additional Grade 3-4 events attributed by the investigator to atezolizumab (n = 1 each, except where indicated): syncope, type 1 diabetes mellitus, anemia, thrombocytopenia/platelet count decreased (n = 3), febrile neutropenia, AST increased, white blood cells decreased (all Grade 3) and pneumonia mycoplasmal (Grade 4) [13].

NEW LEADERS IN BREAST CANCER: PD-L1 AND TARGETED THERAPY

Breast cancer is the most common malignancy in women and it is also the second leading cause of cancer death. A new targeted therapeutic strategy in TNBC is to block the PD-L1/PD-1 axis with checkpoint inhibitors. PD-L1 is a membrane protein that is expressed on multiple cell types. The function of PD-L1 is to activate the immune system and maintain immune tolerance. The PD-L1/PD-1 axis is dysregulated in breast cancer and it is associated with increased tumor antigenicity, reduced tumor infiltration and immune surveillance. The PD-L1/PD-1 axis acts as a negative regulator of T cell function, and it affects the immune system's ability to control cancer.

In a Phase Ib clinical trial, we evaluated the safety and efficacy of atezolizumab in combination with nab-paclitaxel in patients with metastatic TNBC. Atezolizumab is a humanized anti-PD-L1 monoclonal antibody that competitively blocks the PD-L1/PD-1 axis. Nab-paclitaxel is a taxane-based chemotherapy that is used in the treatment of TNBC. Our results demonstrate that the combination of atezolizumab and nab-paclitaxel is safe and effective in patients with mTNBC. The median duration of response (range), months, was 7.1 (1.9 to 11.5). The median overall survival data (all lines) are not yet mature: NE (95% CI, 8.0-NE). Durable confirmed responses were observed in TNBC patients with the combination of atezolizumab and nab-paclitaxel across all lines of therapy. Clinical responses were observed in patients with PD-L1 IC1/2/3 tumors and those with IC0 tumors. Four (13%) patients had a CR, eight (25%) had a PR, and 17 (53%) had a SD. Three patients had a SD lasting > 24 weeks and 17 (53%) had a SD lasting > 12 weeks. Tumors expressing PD-L1 on TC were included in tumors expressing PD-L1 on IC.

REFERENCES

[6] Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; 5Dana-Farber Cancer Institute, Boston, MA; 6Genentech, Inc., South San Francisco, CA; 7Carolina BioOncology Institute, Huntersville, NC.

ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health (NIH) and the National Cancer Institute (NCI). The authors thank the patients and their families who participated in this study and the staff at the participating institutions for their support. AACR 2015 [abstract 2859].