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Can Ipilimumab restore immune response in advanced NSCLC after progression on anti- PD -1/ PD-L1 agents?

AU

Sternschuss, Michal; Peled, Nir; Allen, Aaron M; Dudnik, Elizabeth; Rotem, Ofer; et al.

PUB

Thoracic Cancer 11.8: 2331-2334. John Wiley & Sons, Inc. (Aug 2020)

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AB

Abstract (summary)

Translate [unavailable for this document]

Anti-PD-1/PD-L1 agents play a crucial part in the treatment of non-small cell cancer (NSCLC) demonstrating improved overall response rate (ORR) and overall survival (OS). Recent studies evaluating combination treatment with anti-PD-1 and anti-CTLA-4 suggests improved outcome but also increased toxicity. Evidence is scarce regarding subsequent treatment with immune checkpoint inhibitors (ICPI) after progression on anti-PD-1/PD-L1. A total of 15 patients were treated with a combination of anti-PD1 agent and ipilimumab after confirmed progression of disease on anti-PD1/PDL1 alone during 2017. Clinical data were retrieved retrospectively. Disease control rate (DCR) was defined as partial response (PR) or stable disease (SD). The overall DCR was 33.3% (n = 5); two patients with PR and three patients with SD, three of whom had prior documented disease control on anti-PD1. The immune-related adverse event (irAE) rate was 40% (n = 6); two patients had grade 3 AE and one patient died of pneumonitis. While the median time to progression was two months (range 0.5–16), four of the five patients with PR/SD experienced durable benefit for 8–16 months. This small retrospective cohort of heavily pretreated unselected patients suggests ipilimumab might reboost the immune response in patients with advanced NSCLC following progression of disease on anti-PD1 therapy, while delaying exposure to the higher toxicity rates associated with upfront combination therapy. This strategy should be explored prospectively.

Full text

Translate [unavailable for this document]

Indexing (details)

Cite

SU

Subject

Patients;
Dermatitis;
Histology;
Medical prognosis;
Melanoma;
Immunotherapy;
Chemotherapy;
Disease control

TI

Title

Can Ipilimumab restore immune response in advanced NSCLC after progression on anti- PD -1/ PD-L1 agents?

AU

Author

Sternschuss, Michal [1] ; Peled, Nir [2] ; Allen, Aaron M [1] ; Dudnik, Elizabeth [1] ; Rotem, Ofer [1] ; Kurman, Noga [1] ; Gal, Omer [1] ; Reches, Hiba [1] ; Zer, Alona [3]

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Thoracic Cancer

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BRIEF REPORT

Can Ipilimumab restore immune response in advanced NSCLC after progression on anti-PD-1/PD-L1 agents?

Michal Sternschuss[1], Nir Peled[3,4], Aaron M. Allen[1], Elizabeth Dudnik[1], Ofer Rotem[1], Noga Kurman[1], Omer Gal[1], Hiba Reches[1] & Alona Zer[1,2]

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Keywords
Immune-related adverse events; ipilimumab; nivolumab; NSCLC.

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Abstract

Anti-PD-1/PD-L1 agents play a crucial part in the treatment of non-small cell cancer (NSCLC) demonstrating improved overall response rate (ORR) and overall survival (OS). Recent studies evaluating combination treatment with anti-PD-1 and anti-CTLA-4 suggests improved outcome but also increased toxicity. Evidence is scarce regarding subsequent treatment with immune checkpoint inhibitors (ICPI) after progression on anti-PD-1/PD-L1. A total of 15 patients were treated with a combination of anti-PD1 agent and ipilimumab after confirmed progression of disease on anti-PD1/PDL1 alone during 2017. Clinical data were retrieved retrospectively. Disease control rate (DCR) was defined as partial response (PR) or stable disease (SD). The overall DCR was 33.3% (n = 5); two patients with PR and three patients with SD, three of whom had prior documented disease control on anti-PD1. The immune-related adverse event (irAE) rate was 40% (n = 6); two patients had grade 3 AE and one patient died of pneumonitis. While the median time to progression was two months (range 0.5–16), four of the five patients with PR/SD experienced durable benefit for 8–16 months. This small retrospective cohort of heavily pretreated unselected patients suggests ipilimumab might reboost the immune response in patients with advanced NSCLC following progression of disease on anti-PD1 therapy, while delaying exposure to the higher toxicity rates associated with upfront combination therapy. This strategy should be explored prospectively.

Introduction

Immune checkpoint inhibitors (ICPI) play an increasingly crucial role in the treatment paradigm of metastatic non-small cell lung cancer (mNSCLC) and are now considered the standard of care in both first and advanced lines setting, demonstrating improved objective response rate (ORR) and overall survival (OS) compared with traditional chemotherapy regimens.

Different approaches are being evaluated to maximize treatment efficacy. One approach is combination of inhibitors targeting different immune checkpoints. Anti-programmed death 1 (PD-1) and anticytotoxic T cell lymphocyte-4 (CTLA-4) antibodies have distinct, complementary mechanisms of action and thus, the combination may improve antitumor immunity as demonstrated in other malignancies. A phase 1 study evaluating combination therapy in unselected treatment naïve mNSCLC patients suggested improved ORR and durable responses, at a range of 33%–37% grade 3/4 immune-related adverse events (irAEs).[1] A more recently published phase 3 trial compared combination immunotherapy to standard chemotherapy in patients with a high tumor mutational burden (TMB) and found improved progression-free survival (PFS) and ORR.[2] This trial also reported a grade 3/4 irAE rate of 31.2% as compared with 7%–26% in the major randomized control trials of single agent anti-PD-1/PD-L1.

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Journal title	JN	jn("thoracic cancer")	This is the full journal name (periodical title). A Look-Up list available under Publication title.
Identifier (Keyword)	IF	if(ipilimumab) su(ipilimumab)	These are keywords provided by the authors. They are not available in every document. Searchable with both IF and SU
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