A multidisciplinary characterization of immune-checkpoint inhibitor-related pneumonitis to improve its clinical management

Colucci M[1], Valente M[2], Vegni V[3], Croce V[1], Bellan C[4], Rossi G[2], Gibilisco G[1], Frongia F[1], Danielli R[2], Guazzo R[4], Ghiribelli C[5], Sani T[1], Simonetti E[1], Maio M[1,2], Di Giacomo AM[1,2].

[1]University of Siena, Siena, Italy; [2]Center for Immuno-Oncology, Medical Oncology and Immunotherapy, Department of Oncology, University Hospital of Siena, Siena, Italy; [3]Rugani Hospital, Siena, Italy; [4]Department of Medical Biotechnology, University Hospital of Siena;[5] Interventional and Diagnostic Bronchoscopy, Cardio-Thoracic-Vascular Department, University Hospital of Siena, Siena, Italy

P507

Background

- Treatment with immune checkpoint inhibitors (ICI) can associate with a wide spectrum of immune-related adverse events (irAEs).
- Immune-mediated pneumonitis (im-PN), is a rare but potentially life-threatening side effect.

Methods

- We collected a case series of skin cancer patients (pts) treated with ICI, diagnosed with im-PN (**Tab. 1**).
- Clinical and radiologic data were thoroughly collected, as well as bronchoalveolar lavage (BAL) samples; im-PN were graded using CTCAE v. 5.0.

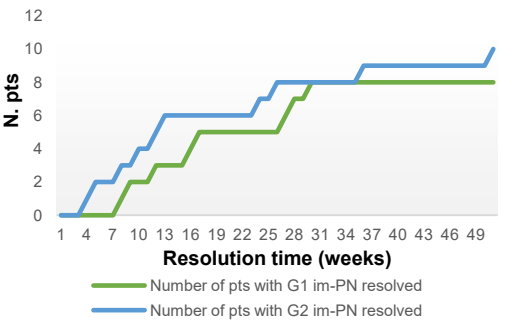
Results

From January 2014 to February 2023, 564 pts with melanoma (n=522) and SCC (n=42) were treated with ICI (349 with anti-PD-1 monotherapy and 215 with combination). Among treated pts, 18 (5%) developed an im-PN.

Table 1. Patients characteristics

Number of patients	18
Median age (range)	67 (41-88)
Gender	
Male	12
Female	6
Tumor histotype	
Melanoma	17
SCC	1
ICI therapy (single agent vs combination therapy)	
Monotherapy	12
Combination	6
im-PN classification (CTCAE v. 5.0)	
G1	8
G2	10

Figure 1. Timing of im-PN resolution



- According to the Fleischner Society classification of drug-related pneumonitis, we identified 3 main radiologic patterns: organizational pneumonia-like (OP) in 10 (55%) pts (**Fig 2A**), pulmonary eosinophilia (Peo) in 7 (39%) pts (**Fig 2B**), and hypersensitivity pneumonitis (HP) in 1 (6%) pt (**Fig 2C**).
- 3/5 pts' BAL samples showed an inflammatory lymphocytic infiltrate, predominantly consisting in a foam cell-like macrophage infiltrate. Notably, Transmission Electron Microscopy (TEM) evaluation performed in 2 out of these 3 pts, revealed the presence of multilamellar bodies, lysosomes (**Fig. 3A**), and lipid vacuoles into the alveolar macrophages (**Fig. 3B**), suggestive for a drug-mediated toxicity.

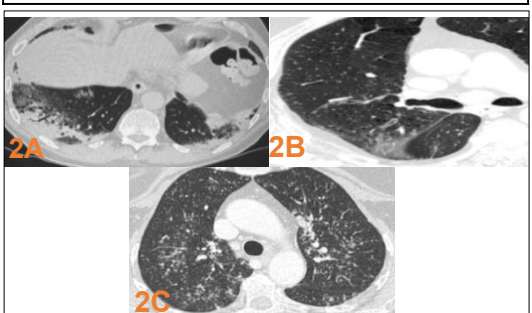


Figure 2. Fleischner Society classification of drug-related pneumonitis

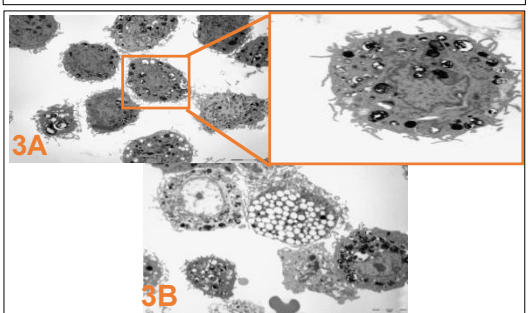


Figure 3. Transmission Electron Microscopy of drug-related pneumonitis

Conclusions

Im-PN associated with ICI therapy was found to be a rare and challenging side effect, with variable onset and heterogenous clinical presentation. A multidisciplinary characterization of im-PN may help optimizing its clinical management to resume ICI therapy.

Email: maura.colucci@student.unisi.it ; 0577 586336