HPR25

Current reimbursement landscape for re-treatment with anti-PD-(L)1 agents after treatment in early-stage cancers: a payer survey

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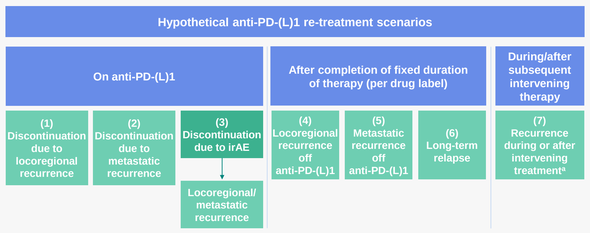
Objectives

Immunotherapies such as those targeting the programmed cell death 1 protein (PD-1) or its ligand, PD-L1 (anti-PD-(L)1s), were initially approved for the treatment of metastatic cancer, having shown substantial clinical benefits in solid tumors. More recently, anti-PD-(L)1s have been approved and used as neoadjuvant and/or adjuvant therapies for early-stage cancers. Current evidence suggests that reintroducing immuno-therapy after its discontinuation can benefit selected patients.[1-3] However, many payers have not articulated reimbursement conditions for re-treatment with anti-PD-(L)1s, while some, such as the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, have followed a “once in a lifetime” criterion for anti-PD-(L)1 therapy. Payer opinions on the definition of re-treatment, as well as the reimbursement of re-treatment by tumor type or by clinical scenarios are unclear; this study aimed to understand their perceptions regarding the definition of re-treatment and the current reimbursement policies for re-treatment with anti-PD-(L)1s following their use in early-stage cancers.

Methods

- An online survey (informed by a targeted literature review) involving 54 payers from France, Germany, Italy, Spain, the UK, the USA, Canada, and Australia, assessed the level of agreement with the following definition of re-treatment: “repeated treatment with the same therapeutic class following relapse after or during neoadjuvant/adjuvant treatment.” The survey also evaluated factors associated with reimbursement decisions for re-treatment with anti-PD-(L)1s following their use in early-stage cancers (triple-negative breast cancer [TNBC], melanoma, non-small cell lung cancer [NSCLC], and renal cell carcinoma [RCC]).
- Seven hypothetical clinical scenarios, reflecting how anti-PD-(L)1 re-treatment is used in practice, were identified and used as stimuli for some questions in the payer survey (Figure 1).

Figure 1: Seven hypothetical clinical scenarios for anti-PD-(L)1 re-treatment



[a]After anti-PD-(L)1 treatment, the patient had taken another treatment. Recurrence/relapse occurred either during this intervening therapy or after completing the intervening treatment. This intervening treatment would not include an anti-PD-(L)1.

Results

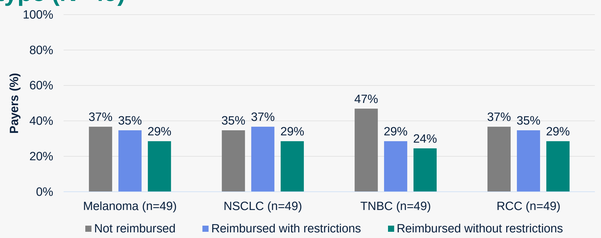
- The sample comprised 59% (32/54) national payers and 41% (22/54) regional/local payers (Table 1).

Table 1: Payers participating in the online survey by type of experience (national vs local)

Country	N	National payer, n (%)	Local payer, n (%)	Mixed national and local, n (%)
USA	5	2 (40)	3 (60)	0 (0)
Canada	8	2 (25)	2 (25)	4 (50)
France	7	6 (86)	1 (14)	0 (0)
Germany	8	6 (75)	2 (25)	0 (0)
Italy	8	3 (38)	4 (50)	1 (0)
Spain	8	1 (13)	6 (75)	1 (13)
UK	8	5 (63)	3 (38)	0 (13)
Australia	2	2 (100)	0 (0)	0 (0)

- The majority of payers agreed with the proposed definition of re-treatment (87%, 47/54).
- The payers’ perceptions of the reimbursement of re-treatment with anti-PD-(L)1s following their use in early-stage cancers was variable in the selected countries, reflecting a similar finding in the earlier targeted literature review. Across tumor types, re-treatment with anti-PD-(L)1s was considered fully reimbursed (by 24%-29% of payers), reimbursed with restrictions (29%-37%), or not reimbursed (35%-47%) (Figure 2).

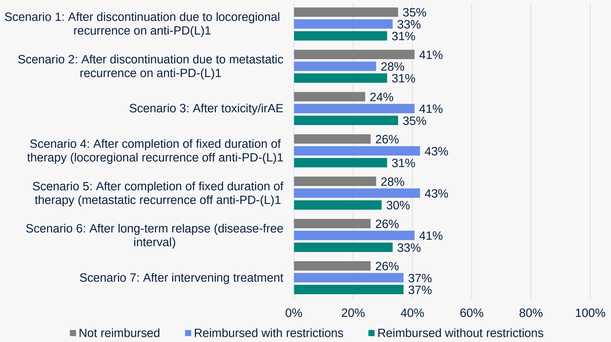
Figure 2: Proportion of payers stating their perception of anti-PD-(L)1 re-treatment reimbursement by tumor type (N=49)[a,b]



[a]The question about reimbursement for re-treatment per tumor type did not clarify whether payers were referring to reimbursement at a national, regional, or local setting. 5 out of the 54 payers did not have experience for the specified tumor types.
[b]Percentages by tumor type may not sum to 100% due to rounding.

- Key reimbursement restrictions mentioned by payers included the length of the disease-free interval from when treatment with an anti-PD-(L)1 for an early-stage cancer was completed (43%), physicians needing to make an individual funding request (33%), and specific restrictions based on the tumor type (26%) or disease stage (24%).
  - For patients who had completed a fixed duration of anti-PD-(L)1 therapy for early-stage cancer (Scenarios 4-6), a disease-free interval of 6 months or longer before considering reimbursement of re-treatment was reported by several payers, predominantly from Canada.
  - Where recurrence occurred after discontinuation due to an immune-related adverse event (irAE; Scenario 3), or completion of a fixed duration of anti-PD-(L)1 therapy (Scenarios 4-6), some payers indicated that a physician had to justify the appropriateness of re-treatment and apply for funding on a case-by-case basis.
  - Across all the scenarios, payers reported reimbursement restrictions for re-treatment if the cancer was considered surgically resectable and/or local.
- Payer responses about the reimbursement status of anti-PD-(L)1 re-treatment varied within each of the seven clinical scenarios. However, scenarios related to recurrence after the completion of a fixed duration of anti-PD-(L)1 (Scenarios 4-6), intervening therapy (Scenario 7), or discontinuation due to toxicity or irAE (Scenario 3) were more frequently reported as reimbursed (73%-76%) than scenarios associated with recurrence during anti-PD-(L)1 therapy (Scenarios 1 and 2; 59%-64%) (Figure 3).

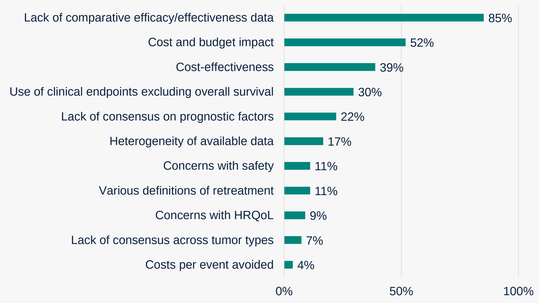
Figure 3: Proportion of payers stating their perception of the reimbursement status of anti-PD-(L)1 re-treatment by clinical scenario (N=54)



[a]Percentages by tumor type may not sum to 100% due to rounding.

- The main barriers to reimbursing re-treatment with anti-PD-(L)1s following their use in early-stage cancers were reported to include a lack of comparative evidence of clinical benefit (85%), cost/budget impact (52%), and cost-effectiveness (39%) (Figure 4). Most payers (70%) reported that access challenges did not differ across tumor types. Some payers stated that if there were any differences, these would be driven by tumor types with greater available evidence on re-treatment (e.g., melanoma).

Figure 4: Proportion of payers reporting the following factors in their three main access challenges/barriers for anti-PD-(L)1 re-treatment (N=54)



Conclusions

Re-treatment with anti-PD-(L)1 therapies is understood by payers as repeated treatment with the same therapeutic class following relapse after or during neoadjuvant/adjuvant treatment. The majority of payers reported reimbursement (with restrictions) of re-treatment in patients initially treated with anti-PD-(L)1s for early-stage cancers. The clinical scenarios in which reimbursement was most frequently reported were in cases of locoregional or metastatic recurrence after the completion of a fixed duration of anti-PD-(L)1 therapy or intervening therapy, and after discontinuation due to toxicity or irAE. Barriers to reimbursement for anti-PD-(L)1 re-treatment by tumor type may differ, as the level of evidence for clinical benefit is linked to when re-treatment for that tumor type was introduced in early-stage cancer settings. Further clinical evidence would be helpful to better inform re-treatment funding decisions.

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