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Atezolizumab (NSCLC, adjuvant 1) –

Addendum to Commission A22-67 (dossier assessment)[1]

Addendum

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Table of contents

List of tables

Page

List of figures

Page

List of abbreviations

Abbreviation	Meaning
AE	adverse event
ALK	anaplastic lymphoma kinase
CTCAE	Common Technology Criteria for Adverse Events
DFS	disease-free survival
EGFR	epidermal growth factor receptor
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
PT	Preferred Term
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)
SOC	System Organ Class

1 Background

On 22 November 2022, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A22-67 (Atezolizumab – Benefit assessment according to §35a Social Code Book V) [1].

The commission comprises the assessment of the data submitted by the pharmaceutical company (hereinafter referred to as "company") in the commenting procedure [2,3] on subsequent therapies, on the time interval between tumour resection and adjuvant chemotherapy, on the epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutation status and on adverse events (AEs) according to threshold values, in each case taking into account the corresponding information in the dossier [4]. In addition, the supplementary assessment was to examine the extent to which the analyses submitted by the company in the commenting procedure address the corresponding points of criticism in IQWiG's benefit assessment. Irrespective of this, a methodological review of the data in the dossier was to be carried out for the outcomes of overall survival and the outcomes on AEs, taking into account the analyses submitted by the company in the commenting procedure, and the results were to be presented.

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The IMpower010 study presented by the company in the dossier was not used for the benefit assessment, as balancing of benefit and risk was not possible on the basis of the analyses presented. In addition, there were further points of criticism concerning the presented patient population (for detailed justification see dossier assessment A22-67 [1]). The analyses subsequently submitted by the company in the commenting procedure have not resolved the relevant points of criticism, so that the analyses of the IMpower010 study remain unsuitable for the benefit assessment. This is justified below. In accordance with the commission, the results of the outcome of overall survival as well as of the outcomes on AEs of the IMpower010 study are methodically reviewed and presented in Appendix B.

2.1 Data on subsequent therapies

With its comments, the company subsequently submitted information on the surgeries and radiotherapies carried out in patients with recurrence (see Table 2). It explains that, especially in the case of locoregional recurrences, surgery or radiation alone can represent an adequate subsequent therapy. However, the data show that in the comparator arm, the majority of surgeries and radiotherapies were carried out for the treatment of distant metastases (correspondingly, the patients had stage IV disease, usually palliative therapy setting) and not for locoregional recurrences. Although it is possible that (as also described by the company) local treatment of the metastases by means of surgery or radiotherapy is initially indicated also for patients with individual distant metastases, it can be assumed that from a certain point onwards in the further progressive course of the disease, subsequent systemic therapy is indicated - with the use of checkpoint inhibitors in the first line in accordance with the guidelines. It must therefore also be criticised that more than 40% of patients with recurrence in the comparator arm did not receive any subsequent systemic therapy at all and more than 50% of patients did not receive any treatment with a checkpoint inhibitor, and that this will not have changed significantly at the 2nd data cut-off [1]. The results in the outcome overall survival are therefore not interpretable, even taking into account the information from the commenting procedure.

2.2 Data on the time interval between tumour resection and adjuvant chemotherapy

In the dossier assessment it was noted that, contrary to the guideline recommendation, in approx. 35% of the patients in the presented subpopulation of the IMpower010 study, there were more than 60 days between tumour resection and adjuvant chemotherapy. Within the framework of its comments, the company provided subgroup analyses for patients with ≤ 60 or > 60 days between tumour resection and adjuvant chemotherapy for the outcomes of overall survival (1st and 2nd data cut-off) and disease-free survival (DFS) (1st data cut-off). Subgroup analyses for the outcomes on side effects are missing. For each of the outcomes of overall survival and DFS, there was no statistically significant effect modification by the characteristic “time interval between tumour resection and adjuvant chemotherapy”. In the group of patients in whom adjuvant chemotherapy was started ≤ 60 days after tumour resection in accordance

with the guidelines, more pronounced effects were seen compared to the group of patients in whom there were more than 60 days between tumour resection and adjuvant chemotherapy. Furthermore, the company submitted analyses from the Clinical Research platform Into molecular testing (CRISP) registry, which show that in some cases, the time interval of 60 days between surgery and chemotherapy is also exceeded in the German healthcare context. However, with 14%, this is much less often the case than in the IMpower010 study with approx. 35%. Overall, however, the point of criticism referred to in the dossier assessment is sufficiently addressed by the company's comments.

2.3 Data on the EGFR and ALK mutation status

It was noted in the dossier assessment that the EGFR and ALK mutation status was unknown in about 45% of the patients in the subpopulation presented. In its comments, the company subsequently submitted information on the EGFR and ALK mutation status. In doing so, the company clarified that approx. 90% of the patients with unknown mutation status had a squamous cell tumour histology. EGFR and ALK mutations are very rare in squamous cell tumours [5], so that a negative mutation status can be assumed in almost all of these patients even without explicit testing. Overall, it is therefore not assumed that a relevant proportion of patients with EGFR or ALK mutation were included in the study in the subpopulation submitted by the company. This point of criticism was thus sufficiently addressed.

2.4 Data on AEs according to threshold values

In Module 4 A of the dossier, the company did not process the AEs at System Organ Class (SOC) and Preferred Term (PT) level according to the threshold values of the dossier template. It subsequently submitted these data with the comments. The subsequently submitted analyses using the threshold values of the dossier template are adequate and are presented, as commissioned, in Appendix D.

2.5 Conclusion

The data subsequently submitted by the company with the comments cannot eliminate the main uncertainties in the subsequent systemic therapies administered, so that the results for the outcome "overall survival" are still not interpretable. The company did not subsequently submit data on DFS or recurrences for the 2nd data cut-off, and no other benefit outcomes, e.g. on symptoms or health-related quality of life, were recorded in the IMpower010 study. Thus, even after the commenting procedure, no usable results on benefit outcomes are available and a balancing of benefit and harm is not possible even taking into account the information from the commenting procedure.

2.6 Summary

The data subsequently submitted by the company in the commenting procedure have not changed the conclusion on the added benefit of atezolizumab from dossier assessment A22-67.

The following Table 1 shows the result of the benefit assessment of atezolizumab under consideration of dossier assessment A22-67 and the present addendum.

Table 1: Atezolizumab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients with completely resected NSCLC at high risk of recurrence after platinum-based chemotherapy whose tumours express PD-L1 in ≥ 50% of the tumour cells and who do not have EGFR mutations or ALK-positive NSCLC; adjuvant treatment	Watchful waiting[b]	Added benefit not proven

a. Presented is the respective ACT specified by the GBA.
b. At the time of application of the therapy to be assessed, the patients are to be considered disease-free. For patients with completely resected NSCLC, there are no approvals or recommendations for further adjuvant drug or non-drug treatment after adjuvant cisplatin-based chemotherapy (and in individual cases, but not regularly, subsequent radiotherapy). Therefore, the G-BA considers watchful waiting as the adequate ACT.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1

The G-BA decides on the added benefit.

3 References

The reference list contains citations provided by the company in which bibliographical information may be missing.

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Appendix A Subsequent antineoplastic therapies (radiation, surgery)

Table 2: Information on subsequent antineoplastic therapies (radiation therapy, surgery) – RCT, direct comparison: atezolizumab versus BSC (IMpower010)

Study **type of subsequent therapy** **localisation**	**Atezolizumab** **N = 106[a]**	**BSC** **N = 103[a]**
IMpower010 (data cut-off 21 January 2021)		
Patients with recurrence	21	43
Patients with at least one radiation therapy, n (%)[b]	10 (47.6)	21 (48.8)
Brain	1 (4.8)	10 (23.3)
Lymph nodes	4 (19.0)	5 (11.6)
Lungs	4 (19.0)	3 (7.0)
Bones	1 (4.8)	4 (9.3)
Other	0 (0)	1 (2.3)
Patients with at least one surgery, n (%)[b]	3 (14.3)	7 (16.3)
Brain	0 (0[c])	6 (14.0[c])
Chest wall	1 (4.8[c])	0 (0[c])
Lungs	2 (9.5[c])	2 (4.7[c])
IMpower010 (data cut-off: 18 April 2022)		
Patients with recurrence	ND[d]	ND[d]
Patients with at least one radiation therapy, n (%)[b]	12 (ND)	24 (ND)
Brain	1 (ND)	12 (ND)
Lymph nodes	6 (ND)	5 (ND)
Lungs	4 (ND)	4 (ND)
Bones	2 (ND)	4 (ND)
Other	0 (0[c])	1 (ND)
Patients with at least one surgery, n (%)[b]	5 (ND)	10 (ND)
Brain	0 (0[c])	6 (ND)
Chest wall	1 (ND)	0 (0[c])
Lungs	3 (ND)	3 (ND)
Lymph nodes	0 (0[c])	1 (ND)
Other	1 (ND)	1 (ND)

a. Number of randomized patients.
c. Based on patients with recurrence.
c. Institute's calculation.
d. For the 2nd data cut-off (18 April 2022), the company presented no data on the number of patients with recurrence.

BSC: best supportive care; n: number of patients with subsequent therapy; N: number of analysed patients; ND: no data; RCT: randomized controlled trial

Appendix B Assessment of the study IMPOWER 010

In the following, the study IMpower010 is assessed according to the commission. Information on study design, interventions administered, available data cut-offs, patient characteristics and subsequent systemic therapies can be found in dossier assessment A22-67. All information refers to the 2nd data cut-off of April 2022.

Planned duration of follow-up observation

Table 3 shows the planned duration of follow-up observation in the IMpower010 study.

Table 3: Planned duration of follow-up observation – RCT, direct comparison: atezolizumab vs. BSC

Study outcome category outcome	Planned follow-up observation
IMpower010	
Mortality	
Overall survival	Until death, lost to follow-up, withdrawal of consent or end of study
Morbidity	
Disease-free survival, recurrence rate[a]	Until the occurrence of a recurrence, death, loss to follow-up, withdrawal of consent or end of study
Health-related quality of life	Outcome not recorded
Side effects	
SAEs and AESIs	Up to 90 days[b] after the last dose of the study medication or initiation of new antineoplastic treatment
Further AEs	Up to 30 days after the last dose of the study medication or initiation of new antineoplastic treatment

a. Comprises the events of local recurrence, regional recurrence, distant recurrence, new primary NSCLC as well as death without recurrence.
b. Before version 4 of the study protocol [5 October 2015] 30 days after the last dose of the study medication or initiation of new antineoplastic treatment.

AE: adverse event; AESI: adverse event of special interest; BSC: best supportive care; NSCLC: non-small cell lung cancer; RCT: randomized controlled trial; SAE: serious adverse event

The observation periods for the outcomes of the category of side effects are systematically shortened because they were only recorded for the time period of treatment with the study medication (plus 30 or 90 days). For these outcomes, data are therefore available only for the shortened observation period. Data on the entire study duration or until death are missing.

However, to be able to draw a reliable conclusion on the total study period or the time to patient death, it would be necessary to record these outcomes as well for the total period, as was done for survival.

Information on the course of the study

Table 4 shows the median/mean treatment durations of the patients and the median/mean observation periods for individual outcomes.

Table 4: Information on the course of the study – RCT, direct comparison: atezolizumab vs. BSC

Study **duration of the study phase** **outcome category**	**Atezolizumab** **N = 106**	**BSC** **N = 103**
IMpower010		
Treatment duration [months]	ND	ND
Observation period [months]		
Overall survival[a]		
Median [Q1; Q3]	49.5 [43.2; 55.0]	46.1 [29.8; 53.7]
Mean (SD)	47.3 (13.2)	41.8 (17.0)
Morbidity (disease-free survival, recurrence rate)	ND	ND
Health-related quality of life	Outcome not recorded	
Side effects		
AEs and severe AEs[b, c]		
Median [Q1; Q3]	11.33 [11.1; 11.7]	12.0 [10.9; 12.3]
Mean (SD)	9.9 (3.6)	10.8 (3.3)
SAEs and AESIs[b, d]		
Median [Q1; Q3]	13.3 [13.0; 13.6]	14.0 [12.9; 14.2]
Mean (SD)	11.8 (3.7)	12.5 (3.6)

a. Calculated as time from randomization to the time point of the 2nd data cut-off, death, loss to follow-up, withdrawal of consent or study discontinuation.
b. Data based on the safety population: N = 104 (intervention) vs. N = 101 (control).
c. Calculated as time since start of treatment until the time point of the 2nd data cut-off, death, loss to follow-up, withdrawal of consent, study discontinuation, until 30 days after the last dose of the study medication or until initiation of a subsequent anticancer therapy.
d. Calculated as time since start of treatment until the time point of the 2nd data cut-off, death, loss to follow-up, withdrawal of consent, study discontinuation, until 90 days after the last dose of the study medication or until initiation of a subsequent anticancer therapy.

AE: adverse event; AESI: adverse events of special interest; BSC: best supportive care; N: number of analysed patients; Q1: 1st quartile; Q3: 3rd quartile; RCT: randomized controlled trial; SAE: serious adverse event SD: standard deviation

There is no information on the treatment duration. The median observation period for the outcome of overall survival was slightly longer in the intervention arm than in the comparator arm. The median observation periods for the outcomes on side effects are comparable between the treatment arms, but markedly shorter compared to “overall survival”.

Outcomes

In accordance with the commission, the following outcomes were assessed:

- Mortality
  - overall survival
- Morbidity
  - recurrence
- Health-related quality of life
- Side effects
  - serious adverse events (SAEs)
  - severe AEs (operationalized as Common Terminology Criteria for Adverse Events [CTCAE] grade ≥ 3)
  - discontinuation due to AEs
  - immune-related SAEs
  - immune-related severe AEs (CTCAE grade ≥ 3)
  - further specific AEs, if any

No usable data were available for the outcomes "recurrence" (represented by DFS and recurrence rate), "immune-related SAEs" and "immune-related severe AEs" (for reasons, see dossier assessment A22-67). Outcomes on symptoms and health-related quality of life were not recorded.

Risk of bias

The risk of bias across outcomes of the IMpower010 study is rated as low.

Due to the insufficient subsequent therapies, the results on the outcome "overall survival" cannot be interpreted (see also Section 2.1 and dossier assessment A22-67). For the outcomes of SAEs severe AEs as well as specific AEs, the risk of bias is rated as high. For the mentioned outcomes of the category of side effects, there are incomplete observations for potentially informative reasons due to the follow-up observation linked to the treatment duration (or the start of a new antineoplastic therapy) and a possible association between outcome and reason for treatment discontinuation. The risk of bias for the results of the outcome of discontinuation due to AEs is rated as low. Despite a low risk of bias, the certainty of results is limited for the outcome of discontinuation due to AEs. Premature treatment discontinuation for reasons other than AEs is a competing event for the outcome to be recorded, discontinuation due to AEs. Consequently, after discontinuation for other reasons, AEs that would have led to discontinuation may have occurred, but the criterion of discontinuation could no longer be applied to them. It is impossible to estimate how many AEs are affected by this issue.

Results

Table 5 and Table 6 summarize the results of the IMpower010 study. Kaplan-Meier curves can be found in Appendix C, tables on common AEs are presented in Appendix D.

Table 5: Results (mortality, morbidity; health-related quality of life) – RCT, direct comparison: atezolizumab vs. BSC

Study outcome category outcome	Atezolizumab		BSC		Atezolizumab vs. BSC
	N	median time to event in months [95% CI] patients with event n (%)	N	median time to event in months [95% CI] patients with event n (%)	HR [95% CI][a]; p-value[b]
IMpower010 (data cut-off: 18 April 2022)					
Mortality					
Overall survival	106	NA 15 (14.2)	103	NA 30 (29.1)	0.45 [0.24; 0.85]; 0.012
Morbidity					
Recurrence	No usable data[c]				
Health-related quality of life	No outcomes recorded in this category				

a. Cox proportional hazards model stratified by sex, tumour histology and disease stage.
b. Log-rank test, two-sided.
c. For reasons, see dossier assessment A22-67 [1].

BSC: best supportive care; CI: confidence interval; HR: hazard ratio; n: number of patients with event; N: number of analysed patients; NA: not achieved; RCT: randomized controlled trial

Table 6: Results (side effects) – RCT, direct comparison: atezolizumab vs. BSC

Study outcome category outcome	Atezolizumab N	Atezolizumab patients with event n (%)	BSC N	BSC patients with event n (%)	Atezolizumab vs. BSC RR [95% CI]; p-value[a]
IMpower010 (data cut-off 18 April 2022)					
Side effects					
AEs (supplementary information)	104	99 (95.2)	101	71 (70.3)	–
SAEs	104	16 (15.4)	101	4 (4.0)	3.88 [1.34; 11.22]; 0.006
Severe AEs[b]	104	21 (20.2)	101	11 (10.9)	1.85 [0.94; 3.65]; 0.070
Discontinuation due to AEs	104	20 (19.2)	101	0 (0)	39.83 [2.44; 649.84]; < 0.001
Immune-related AEs (AEs, SAEs, severe AEs)				No usable data[c]	
Fever (PT, AEs)	104	11 (10.6)	101	0 (0)	22.34 [1.33; 374.20]; < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)	104	36 (34.6)	101	6 (5.9)	5.83 [2.57; 13.23]; < 0.001
Infections and infestations (SOC, SAEs)	104	7 (6.7)	101	0 (0)	–; 0.008[d]

a. Institute's calculation of RR, CI (asymptotic) and p-value (unconditional exact test, CSZ method according to [6]). In case of 0 events in one study arm, the correction factor 0.5 was used for the calculation of effect and CI in both study arms.
b. Operationalized as CTCAE grade ≥ 3.
c. For reasons, see dossier assessment A22-67 [1].
d. No presentation of effect estimation and CI as these are not informative.

AE: adverse event; BSC: best supportive care; CI: confidence interval; CSZ: convexity, symmetry, z-score; CTCAE: Common Terminology Criteria for Adverse Events; n: number of patients with (at least one) event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; RR: relative risk; SOC: System Organ Class; SAE: serious adverse event

Mortality

Overall survival

For the outcome "overall survival", there is a statistically significant advantage for atezolizumab over BSC.

Morbidity

Recurrence

There were no usable data for the outcome "recurrence".

Health-related quality of life

Outcomes on health-related quality of life were not recorded.

Side effects

SAEs

A statistically significant disadvantage of atezolizumab in comparison with BSC was shown for the outcome SAEs.

Severe AEs (CTCAE grade ≥ 3)

No statistically significant difference between the treatment arms was shown for the outcome "severe AEs (CTCAE grade ≥ 3)".

Discontinuation due to AEs

A statistically significant disadvantage of atezolizumab versus BSC was shown for the outcome "discontinuation due to AEs".

Specific AEs

Immune-related SAEs and immune-related severe AEs

For the outcomes “immune-related SAEs” and “immune-related severe AEs”, no usable data were available.

Further specific AEs (fever [PT, AEs], skin and subcutaneous tissue disorders [SOC, AEs], infections and infestations [SOC, SAEs])

A statistically significant disadvantage of atezolizumab in comparison with BSC was shown for each of the outcomes “fever” (PT, AEs), “skin and subcutaneous tissue disorders” (SOC, AEs) and “infections and infestations” (SOC, SAEs).

Subgroups and other effect modifiers

The following potential effect modifiers were considered for the present assessment:

- Age (< 65 years versus ≥ 65 years)
- Sex (male versus female)
- Tumour stage (IIA vs. IIB vs. IIIA)

Interaction tests are performed if at least 10 patients per subgroup are included in the analysis. Moreover, for binary data, there had to be 10 events in at least one subgroup.

Only results showing an effect modification with a statistically significant interaction between treatment and subgroup characteristic (p-value < 0.05) are presented. In addition, subgroup results are presented only if there is a statistically significant and relevant effect in at least one subgroup.

There were no relevant effect modifiers.

Appendix C Kaplan-Meier curves

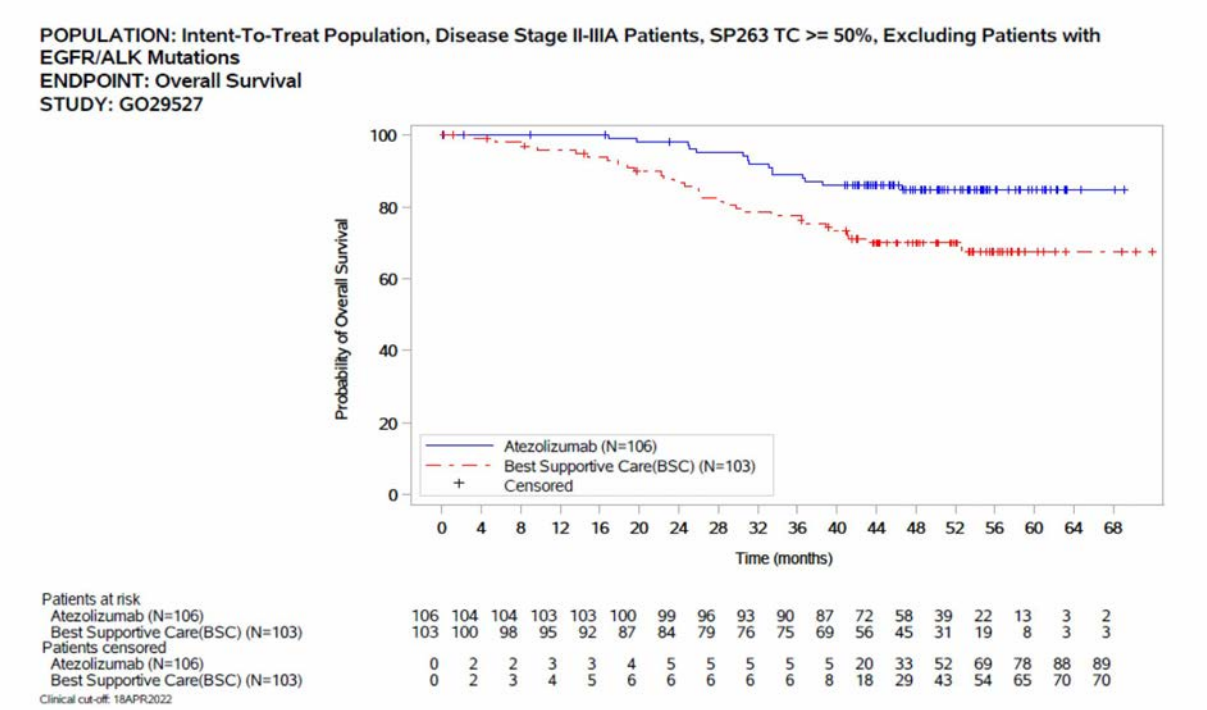

Figure 1: Kaplan-Meier curves on the outcome “overall survival” in the IMpower010 study (data cut-off: April 2022)

Appendix D Results on side effects

For the overall rates of AEs, SAEs, and severe AEs (CTCAE grade ≥ 3), the following tables present events for SOCs and PTs according to the Medical Dictionary for Regulatory Activities (MedDRA), each on the basis of the following criteria:

- overall rate of AEs (irrespective of severity grade): events which occurred in at least 10% of patients of 1 study arm
- overall rates of severe AEs (CTCAE grade ≥ 3) and SAEs: events that occurred in at least 5 % of the patients in one study arm
- in addition, for all events irrespective of severity grade: events which occurred in at least 10 patients and in at least 1% of patients in 1 study arm

For the outcome "discontinuation due to AEs", a complete presentation of all events (SOCs/PTs) that resulted in discontinuation is provided.

Table 7: Common AEs[a] – RCT, direct comparison: atezolizumab vs. BSC

Study	Patients with event n (%)	
SOC[b] PT[b]	atezolizumab N = 104	BSC N = 101
IMpower010 (data cut-off 18 April 2022)		
Overall AE rate	99 (95.2)	71 (70.3)
Blood and lymphatic system disorders	12 (11.5)	7 (6.9)
Endocrine disorders	17 (16.3)	2 (2.0)
Hypothyroidism	11 (10.6)	0 (0)
Gastrointestinal disorders	23 (22.1)	12 (11.9)
General disorders and administration site conditions	25 (24.0)	12 (11.9)
Pyrexia	11 (10.6)	0 (0)
Infections and infestations	45 (43.3)	35 (34.7)
Nasopharyngitis	8 (7.7)	13 (12.9)
Investigations	34 (32.7)	9 (8.9)
Metabolism and nutritional disorders	20 (19.2)	12 (11.9)
Musculoskeletal and connective tissue disorders	31 (29.8)	17 (16.8)
Arthralgia	13 (12.5)	5 (5.0)
Nervous system disorders	26 (25.0)	23 (22.8)
Respiratory, thoracic, and mediastinal disorders	31 (29.8)	20 (19.8)
Cough	15 (14.4)	10 (9.9)
Skin and subcutaneous tissue disorders	36 (34.6)	6 (5.9)
Pruritus	12 (11.5)	2 (2.0)

a. Events that occurred in ≥ 10 patients in at least one study arm.
b. MedDRA version 23.1; SOC and PT notation taken from the subsequently submitted data from the comments.

AE: adverse event; BSC: best supportive care; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SOC: System Organ Class

Table 8: Common SAEs[a] – RCT, direct comparison: atezolizumab vs. BSC

Study	Patients with event n (%)	
SOC[b] PT[b]	atezolizumab N = 104	BSC N = 101
IMpower010 (data cut-off: 18 April 2022)		
Total SAE rate	16 (15.4)	4 (4.0)
Infections and infestations	7 (6.7)	0 (0)

a. Events that occurred in ≥ 5% of the patients in at least 1 study arm.
b. MedDRA version 23.1; SOC and PT notation taken from the subsequently submitted data from the comments.

BSC: best supportive care; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SAE: serious adverse event; SOC: System Organ Class

Table 9: Common severe AEs (CTCAE grade ≥ 3)[a] – RCT, direct comparison: atezolizumab vs. BSC

Study	Patients with event n (%)	
	atezolizumab N = 104	BSC N = 101
IMpower010 (data cut-off: 18 April 2022)		
Overall rate of severe AEs (CTCAE grade ≥ 3)[b]	21 (20.2)	11 (10.9)

a. Events that occurred in ≥ 5% of the patients in at least 1 study arm.
b. For severe AEs, no MedDRA SOCs and PTs met the criterion for presentation.

AE: adverse event; BSC: best supportive care; CTCAE: Common Terminology Criteria for Adverse Events; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SOC: System Organ Class

Table 10: Discontinuation due to AEs – RCT, direct comparison: atezolizumab vs. BSC

Study	Patients with event n (%)	
SOC[a] **PT[a]**	**atezolizumab N = 104**	**BSC N = 101**
IMpower010 (data cut-off: 18 April 2022)		
Total rate of discontinuations due to AEs	20 (19.2)	0 (0)
Blood and lymphatic system disorders	1 (1.0)	0 (0)
Sarcoidosis of lymph node[b]	1 (1.0)	0 (0)
Cardiac disorders	2 (1.9)	0 (0)
Atrial fibrillation	1 (1.0)	0 (0)
Cardiac failure	1 (1.0)	0 (0)
Endocrine disorders	2 (1.9)	0 (0)
Hypothyroidism	2 (1.9)	0 (0)
Gastrointestinal disorders	1 (1.0)	0 (0)
Colitis	1 (1.0)	0 (0)
Hepatobiliary disorders	3 (2.9)	0 (0)
Drug-induced liver injury	1 (1.0)	0 (0)
Hepatic function abnormal	2 (1.9)	0 (0)
Immune system disorders	1 (1.0)	0 (0)
Hypersensitivity	1 (1.0)	0 (0)
Infections and infestations	2 (1.9)	0 (0)
Encephalitis	1 (1.0)	0 (0)
Meningitis	1 (1.0)	0 (0)
Investigations	2 (1.9)	0 (0)
Alanine aminotransferase increased	1 (1.0)	0 (0)
Aspartate aminotransferase increased	1 (1.0)	0 (0)
Blood creatinine increased	1 (1.0)	0 (0)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	1 (1.0)	0 (0)
Renal neoplasm	1 (1.0)	0 (0)
Respiratory, thoracic and mediastinal disorders	5 (4.8)	0 (0)
Interstitial lung disease	1 (1.0)	0 (0)
Lung disorders	1 (1.0)	0 (0)
Pneumonitis	3 (2.9)	0 (0)

a. MedDRA version 23.1; SOCs and PTs taken from Module 4.
b. This event, defined by the company as PT, does not exist in MedDRA.

AE: adverse event; BSC: best supportive care; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SOC: System Organ Class