NSCLC

STAGE II-III NSCLC

IMFINZI®: The solution for curative-intent treatment of stage II-III NSCLC[1,+]

AEGEAN: IMFINZI®

as the **first approved** perioperative immunotherapy for resectable stage II-III NSCLC patients[2]

PACIFIC: IMFINZI®

as **standard of care** for stage III unresectable NSCLC patients[3,4]

AstraZeneca

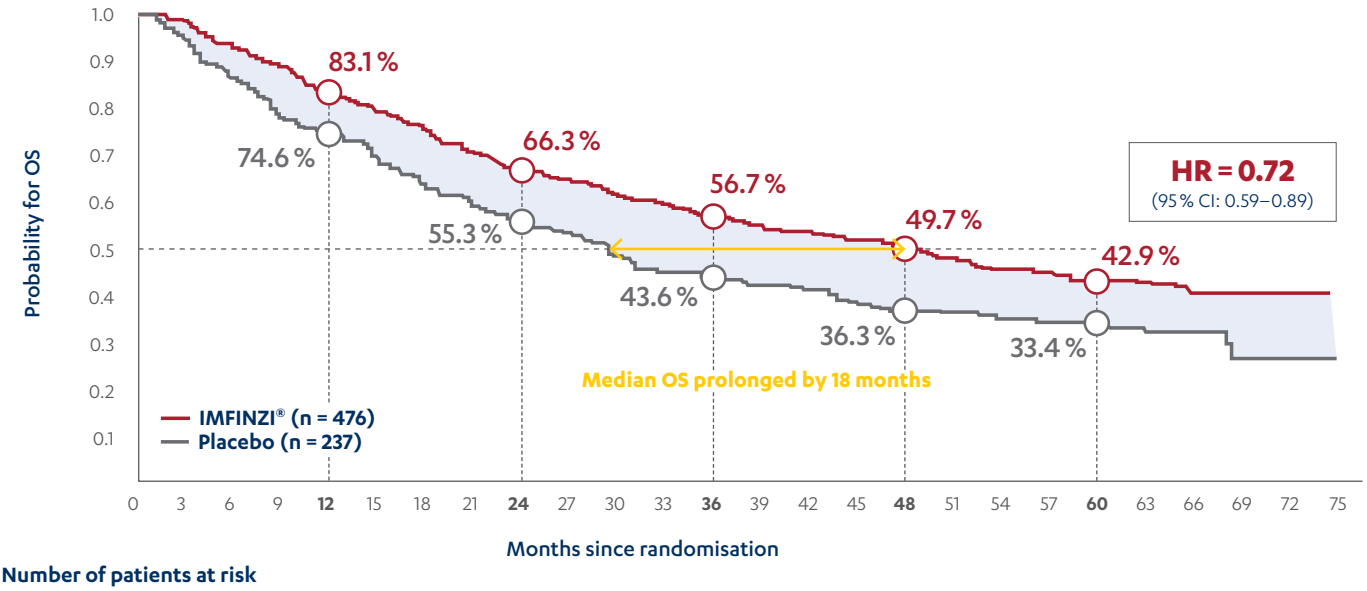
IMFINZI® durvalumab

PACIFIC: SoC for stage III unresectable NSCLC patients[3, 4]

Study design:[5]

- PACIFIC is a phase 3, international, randomized, double-blind trial comparing IMFINZI® with placebo in patients with stage III unresectable NSCLC that had not progressed after platinum-based CRT
- Primary endpoints comprise OS and PFS by BICR

Sustained 5-year survival benefit with IMFINZI®[6]



Number of patients at risk

IMFINZI®	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

Adapted according to Spigel et al., 2021.[6]

- 28 % reduction in risk of mortality[6]
- 18 month longer median overall survival with IMFINZI® versus placebo[6]

PACIFIC: The only approved and reimbursed immunotherapy for stage III unresectable NSCLC after CRT[2, 7]

1× monthly maintenance therapy - every 4 weeks[2, §]

IMFINZI® 1,500 mg — **60-minute infusion** — **Every 4 weeks**

1 year/13 cycles

Curative-intent therapy in UR NSCLC

PACIFIC →

- Concurrent Chemo-radiotherapy → IMFINZI®
- Sequential Chemo-radiotherapy → IMFINZI®

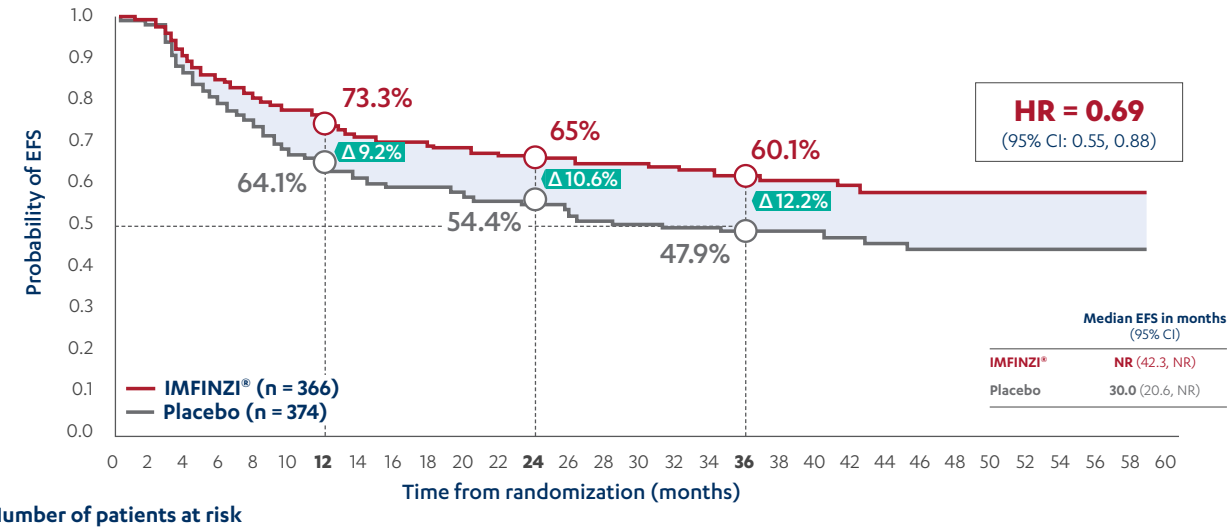
NCCN Guideline recommendation:
IMFINZI® is recommended after CRT for eligible patients with unresectable stage III NSCLC[3]

AEGEAN: First Swiss approved and to date only approved perioperative study for stage II-III resectable NSCLC[2]

Study design:[8]

- AEGEAN is a phase 3, global, randomized, double-blind, placebo-controlled study evaluating perioperative IMFINZI® + neoadjuvant CT in patients with stage II-III resectable NSCLC
- Primary endpoints include pCR by central lab and EFS using BICR†

Significant improvement in EFS* with IMFINZI®[9]



Number of patients at risk

IMFINZI®	366	337	276	240	219	201	194	179	172	128	121	76	67	48	36	29	6	4	4	4	0
Placebo	374	338	261	225	201	176	172	151	142	93	83	57	53	36	32	25	8	3	2	2	0

Data cut-off: May 10, 2024

Adapted according to Heymach JV et al., 2024.[9]

39.1% maturity and 25.9 months median follow-up in censored patients.

- 31 % reduction in the risk of an EFS event[9]
- 4 × higher pathologic complete response rate[8]

Perioperative IMFINZI® + neoadjuvant CT is a new treatment option for patients with resectable NSCLC[2]

Neoadjuvant IMFINZI® + CT Q3W,

followed by only one administration of adjuvant IMFINZI® per month[2]

Neoadjuvant: Q3W × 4 CYCLES | **Adjuvant: Q4W × 12 CYCLES**

IMFINZI® 1,500 mg** + **Platinum-based CT#** → Surgery → **IMFINZI®** 1,500 mg**

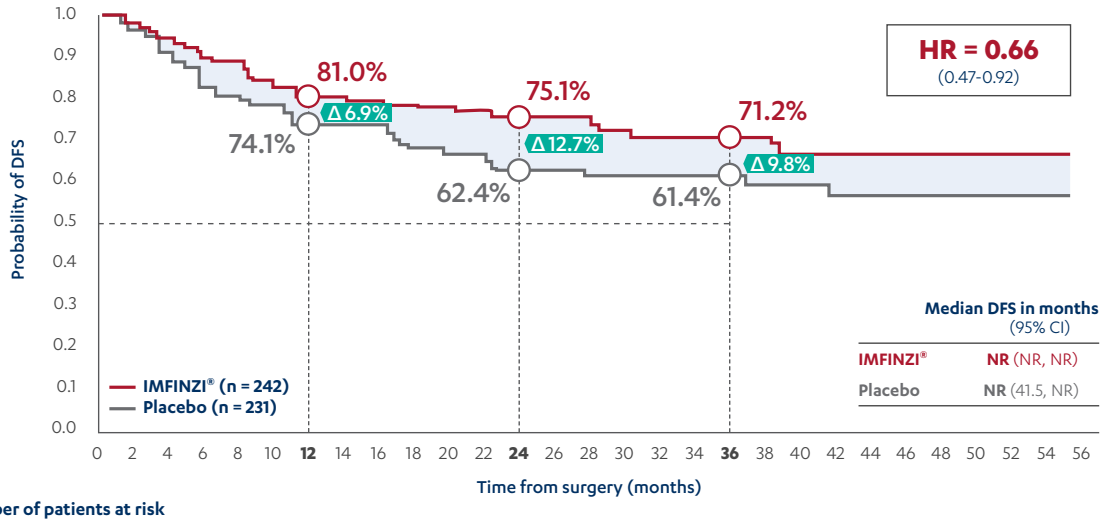
Curative-intent therapy in rNSCLC — AEGEAN → **IMFINZI®** + Chemotherapy → Surgery → **IMFINZI®**

NCCN Guideline recommendation: **Perioperative therapy** should be given as a **single regimen** and change of immunotherapy is not recommended[3]

IMFINZI®: First Swiss approved perioperative immunotherapy for resectable stage II-III NSCLC[2]

STAGE II-III rNSCLC

Clinically meaningful* DFS[##] benefit with IMFINZI®[9]



Number of patients at risk

IMFINZI®	242	226	201	186	171	168	155	151	113	110	65	61	45	27	26	4	4	4	4	0
Placebo	231	212	185	172	152	150	125	122	74	71	46	45	31	23	21	3	2	2	2	0

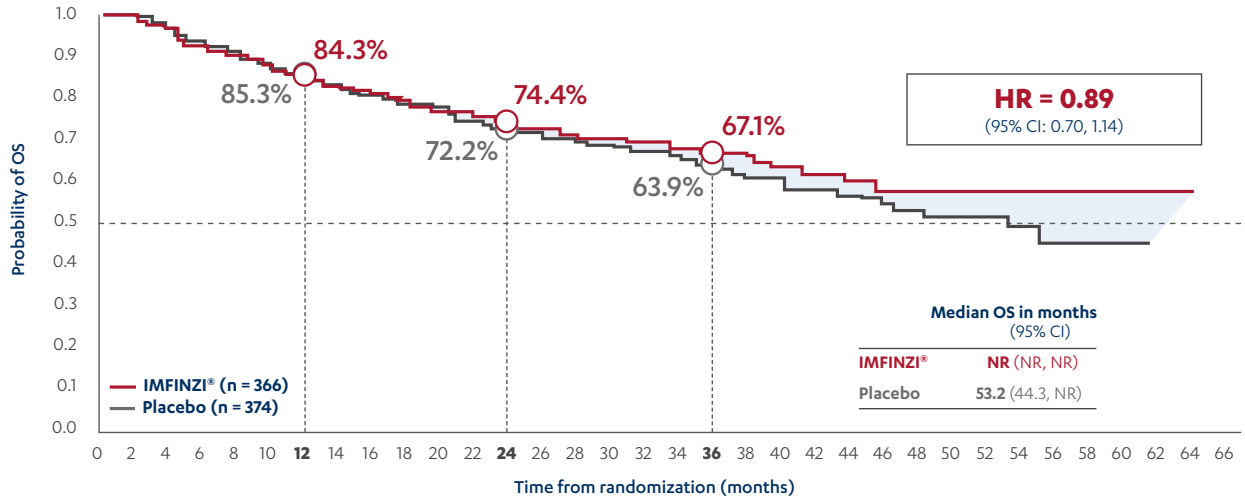
Data cut-off: May 10, 2024

Adapted according to Heymach JV et al., 2024.[9]

* The critical HR of 0.654 to reach statistical significance was not met.[9]
29.8% maturity and 27.3 months median follow-up in censored patients.

> 70% of patients treated with IMFINZI® remain disease-free after 3 years[9]

Positive OS trend for IMFINZI® vs placebo[9§§]



Number of patients at risk

IMFINZI®	366	356	327	316	297	288	277	267	260	227	182	141	104	80	62	50	39	29	16	12	3	1	0
Placebo	374	367	342	327	309	292	287	270	259	230	183	149	116	87	68	58	41	28	16	7	2	0	0

Data cut-off: May 10, 2024

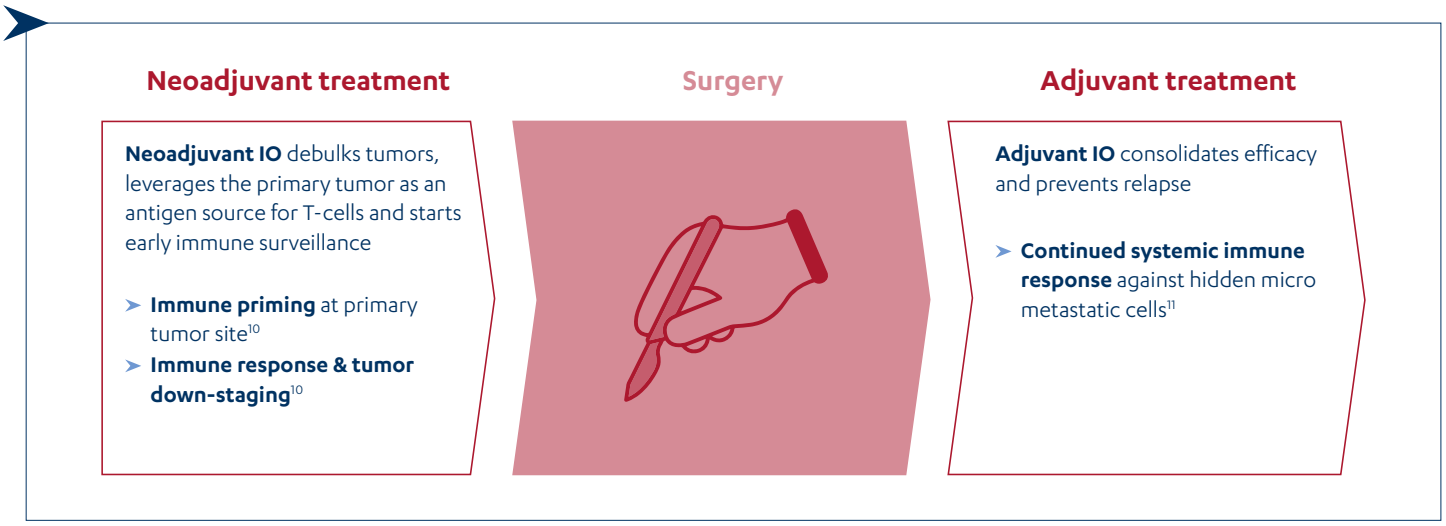
Adapted according to Heymach JV et al., 2024.[9]

According to AEGEAN statistical planning, overall survival (OS) could not be formally evaluated due to the lack of statistical significance in disease-free survival (DFS).
35.3% maturity and 33.6 months median follow up in censored patients.

At interim analysis II, the AEGEAN data indicates a positive OS trend with a HR of 0.89 (95% CI: 0.70-1.14)[9]

The median OS in the placebo group was 53.2 month, but has not yet been reached in the IMFINZI® arm.[9]

Rationale for AEGEAN: Perioperative immunotherapy



➤ Perioperative treatments may provide complementary benefits in reducing tumour volume in neoadjuvant setting and mitigate recurrence risk in adjuvant setting[10,11]

AEGEAN: First phase 3 study to describe the benefits of perioperative immunotherapy + neoadjuvant CT[8,9]

➤ **Clinically meaningful DFS benefit** (HR: 0.66; 95% CI: 0.47-0.92)[9]

➤ **Positive OS trend:** IMFINZI® is the only perioperative IO treatment showing a **30% reduction in lung cancer-related death**[9]

➤ Perioperative IMFINZI® + neoadjuvant CT is associated with a **manageable AE profile**, with **no new safety signals** observed[8,9]

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† IMFINZI® in combination with platinum-based chemotherapy as neoadjuvant treatment, followed by IMFINZI® as monotherapy after surgery, is indicated for the treatment of adult patients with resectable (tumours ≥ 4 cm and/or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.[2]

§ Patients weighing 30 kg or less must be given a dose based on body weight, equivalent to 10 mg/kg IMFINZI® every 2 weeks or 20 mg/kg every 4 weeks as a monotherapy until body weight has increased to above 30 kg.[2]

† All efficacy analyses were performed on a modified population that excludes patients with documented EGFR/ALK aberrations.[8]

* EFS was defined as the time from randomization to the earliest of the following: progressive disease that precluded surgery, progressive disease that was discovered and reported by the investigator when attempting surgery and that prevented completion of the surgery, local or distant recurrence using BICR per RECIST v1.1, or death from any cause.[9]

Administer IMFINZI® on the same day before chemotherapy. Please also refer to the Information for Healthcare Professionals for chemotherapy agents for information on the dosage.[2]

** The dosage must be adjusted to body weight in patients weighing 30 kg or less, equivalent to 20 mg/kg IMFINZI® in combination with chemotherapy every 3 weeks (21 days) for 4 cycles, followed by 20 mg/kg every 4 weeks as a monotherapy until body weight increases to above 30 kg.[2]

DFS was defined as the time from the date of surgery until the first date of disease recurrence (local or distant), or date of death due to any cause, whichever occurs first. DFS was analyzed in patients in the mITT population who had tumor resection with R0/R1 margins and no evidence of disease in the first post-surgery scan.[9]

§§ OS was defined as the time from randomization to death due to any cause.[9]

AE: adverse event; **ALK:** anaplastic lymphoma kinase; **BICR:** Blinded independent central review; **CI:** confidence interval; **CT:** chemotherapy; **CRT:** chemoradiation therapy; **DFS:** disease-free survival; **EFS:** event-free survival; **EGFR:** epidermal growth factor receptor; **HR:** hazard ratio; **IO:** immuno-oncology; **mITT:** modified intent-to-treat; **NCCN:** National Comprehensive Cancer Network; **NR:** not reached; **NSCLC:** non-small cell lung cancer; **OS:** overall survival; **pCR:** pathologic complete response; **PFS:** progression-free survival; **Q3W:** every 3 weeks; **Q4W:** every 4 weeks; **R0:** no residual tumor; **R1:** microscopic residual tumor; **RECIST v1.1:** Response Evaluation Criteria in Solid Tumors version 1.1; **rNSCLC:** resectable NSCLC; **SoC:** standard of care; **UR:** unresectable.

References:

1. Mitsudomi T, et al. Surgical outcomes with neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in resectable NSCLC (AGEAN) [presentation]. Presented at: World Conference on Lung Cancer (WCLC); September 9-12, 2023; Singapore. **2.** IMFINZI® Information for Healthcare Professionals. www.swissmedicinfo.ch. **3.** NCCN Guidelines, online available: https://www.nccn.org/professionals/physician_gls/pdf/NSCLC.pdf (last access: 07.05.2024). **4.** ESMO Guidelines, online available: https://www.esmo.org/guidelines/guidelines-by-topic/lung-and-chest-tumours (last access: 07.05.2024). **5.** Antonia SJ, et al. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. N Engl J Med. 2018; 379(24): 2342–2350. **6.** Spigel DR, et al. Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. J Clin Oncol. 2022; 40 (12): 1301–1311. **7.** List of specialities. www.spezialitätenliste.ch. **8.** Heymach JV, et al. Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer. N Engl J Med. 2023 Nov 2;389(18):1672-1684. (Including supplementary appendix). **9.** Heymach JV, Harpole D, Mitsudomi T, et al. Perioperative Durvalumab for Resectable NSCLC: Updated Outcomes from the Phase 3 AEGEAN Trial [presentation]. Presented at: World Conference on Lung Cancer (WCLC); Sep 7-10, 2024; San Diego, CA. **10.** Forde PM, et al. Neoadjuvant PD-1 Blockade in Resectable Lung Cancer. N Engl J Med. 2018 May 24;378(21):1976-1986. **11.** Peng Y, et al. Progress and perspectives of perioperative immunotherapy in non-small cell lung cancer. Front Oncol. 2023 Jan 25;13: 1011810.

Imfinzi®

Comp: Durvalumab; concentrate for solution for infusion; 50 mg/mL; List A. **Ind:** For the treatment of adult patients with locally advanced, unresectable non-small cell lung cancer (NSCLC) whose disease has not progressed following definitive platinum-based chemoradiation therapy. In combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC). In combination with platinum-based chemotherapy as neoadjuvant treatment, followed by Imfinzi as monotherapy after surgery, is indicated for the treatment of adult patients with resectable (tumours ≥ 4 cm and/or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements. In combination with gemcitabine and cisplatin for the first line treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC). **Dos:** *Locally Advanced NSCLC:* 10 mg/kg every 2 weeks or 1500 mg every 4 weeks for a maximum of 12 months. *Resectable NSCLC:* 1500 mg every 3 weeks for up to 4 cycles prior to surgery, followed by 1500 mg every 4 weeks for a maximum of 12 cycles after surgery *ES-SCLC:* 1500 mg every 3 weeks (21 days) for 4 cycles, followed by 1500 mg every 4 weeks. *BTC:* 1500 mg every 3 weeks (21 days) for up to 8 cycles, followed by 1500 mg every 4 weeks. **CI:** Hypersensitivity to the active substance or to any of the excipients. **W&P:** Immune-mediated ADRs (pneumonitis, hepatitis, colitis, nephritis, rash, myocarditis, haemophagocytic lymphohistiocytosis (HLH)), immune-mediated endocrinopathies (hypothyroidism, hyperthyroidism, thyroiditis, adrenal insufficiency, type 1 diabetes mellitus, hypophysitis/hypopituitarism), aseptic meningitis, haemolytic anaemia, immune thrombocytopenia, cystitis noninfective, myositis, rhabdomyolyses, encephalitis, pancreatitis, Guillain-Barré syndrome, arthritis, uveitis and ocular inflammatory toxicity, polymyositis, myasthenia gravis, infusion-related reactions, adverse reactions in transplant recipients, cerebrovascular events. **IA:** Corticosteroids and immunosuppressants before starting treatment. **ADRs:** *Monotherapy:* Very common: upper respiratory tract infections, cough/productive cough, diarrhoea, abdominal pain, rash, pruritus, pyrexia. Common: pneumonia, oral candidiasis, dental and oral soft tissue infections, hypothyroidism, influenza, hyperthyroidism, TSH increased, pneumonitis, dysphonia, hepatitis, aspartate aminotransferase increased or alanine aminotransferase increased, night sweats, myalgia, blood creatinine increased, dysuria, peripheral oedema, infusion related reaction. *In combination with chemotherapy:* Very common: neutropenia, anaemia, thrombocytopenia, leukopenia, decreased appetite, insomnia, cough/productive cough, nausea, constipation, vomiting, diarrhoea, abdominal pain, aspartate aminotransferase increased or alanine aminotransferase increase, alopecia, rash, pruritus, fatigue, pyrexia. Common: upper respiratory tract infections, influenza, pneumonia, dental and oral soft tissue infections, sepsis, febrile neutropenia, pancytopenia, hypothyroidism, hyperthyroidism, adrenal insufficiency, TSH increased, hypomagnesaemia, hypokalaemia, hyponatraemia, dehydration, hypocalcaemia, cerebrovascular events, neuropathy peripheral, headache, tinnitus, tachycardia, hypotension, pneumonitis, dysphonia, dyspnoea, pulmonary embolism, hiccups, stomatitis, amylase increased, hepatitis, blood bilirubin increased, gamma-glutamyltransferase increased, blood creatinine increased, dysuria, acute kidney injury, proteinuria, dermatitis, back pain, myalgia, muscle spasms, peripheral oedema, chills, oedema, malaise, infusion related reaction. Uncommon, rare, very rare, unknown: see www.swissmedicinfo.ch. Date of revision of the text: May 2024. Further information: www.swissmedicinfo.ch or AstraZeneca AG, Neuhofstrasse 34, 6340 Baar, Switzerland. www.astrazeneca.ch.
Professionals can request the mentioned references to AstraZeneca AG.

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