Durvalumab (Imfinzi®) as monotherapy for the first line treatment of advanced or unresectable hepatocellular carcinoma (HCC)

General information

Drug description [1]

Durvalumab (Imfinzi®) is a fully human, immunoglobulin G1 kappa monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80. Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.

Indication [2]

Durvalumab (Imfinzi®) as monotherapy is indicated for the first line treatment of adults with advanced or unresectable HCC.

Incidence

- In Austria, in 2020, a total of 995 patients were newly diagnosed with liver cancer. The age-standardised incidence rate[1] was 17.0 per 100,000 men and 6.0 per 100,000 women [3].
- HCC constitutes more than 90% of the primary tumour of the liver. HCC occurs in approximately 85% of patients diagnosed with cirrhosis.
- HCC is now the fifth most common cause of cancer worldwide and the second leading cause of cancer death after lung cancer in men [4].

Current treatment [5]

- NICE[2] recommends the following treatment options for advanced (stage B not eligible for locoregional therapy or stage C) HCC:
  - Lenvatinib is recommended as an option for untreated, advanced, unresectable HCC in adults.
  - Sorafenib is recommended as an option for treating advanced HCC only for people with Child-Pugh grade A liver impairment.

Regulatory status

EMA [2]

Approval status for this indication: On 12 October 2023, the CHMP adopted a positive opinion recommending a change to the terms of the marketing authorisation for Imfinzi®.

<u>The CHMP adopted a new indication as follows:</u>

- Imfinzi® as monotherapy is indicated for the first-line treatment of adults with advanced or unresectable HCC.

Other indications: Imfinzi® is indicated:

- as monotherapy for the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.
- in combination with tremelimumab and platinum-based chemotherapy for the first-line treatment of adults with metastatic NSCLC with no sensitising EGFR mutations or ALK-positive mutations.
- in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC).
- in combination with gemcitabine and cisplatin for the first-line treatment of adults with unresectable or metastatic biliary tract cancer (BTC).
- in combination with tremelimumab for the first-line treatment of adults with advanced or unresectable HCC.

✓ **Medicine under additional monitoring**

FDA [6]

Approval status for this indication: not approved.

Other indications: Imfinzi® is indicated:

- for the treatment of adult patients with unresectable, Stage III NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.
- in combination with tremelimumab-actl and platinum-based chemotherapy, for the treatment of adult patients with metastatic NSCLC with no sensitizing EGFR mutations or ALK genomic tumour aberrations.
- in combination with etoposide and either carboplatin or cisplatin, as first-line treatment of adult patients with ES-SCLC.
- in combination with gemcitabine and cisplatin, as treatment of adult patients with locally advanced or metastatic BTC.
- in combination with tremelimumab-actl, for the treatment of adult patients with unresectable HCC.

[1] European standard Population 2013.
[2] Currently, there is no Onkopedia guideline available for HCC.

Manufacturer

Imfinzi® is manufactured by AstraZeneca.

Costs

10 ml Imfinzi® concentrate for solution for infusion 50mg/ml = € 3,088.00 (ex-factory price) [7]

Warnings and precautions [1]

- **Traceability**
  - In order to improve the traceability of biological medicinal products, the tradename and the batch number of the administered product should be recorded.
- **Immune-mediated pneumonitis**
  - Immune-mediated pneumonitis or interstitial lung disease (ILD), defined as requiring the use of systemic corticosteroids and with no clear alternate aetiology, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab.
- **Pneumonitis and radiation pneumonitis**
  - Radiation pneumonitis is frequently observed in patients receiving radiation therapy to the lung and the clinical presentation of pneumonitis and radiation pneumonitis is very similar.
  - Patients should be monitored for signs and symptoms of pneumonitis or radiation pneumonitis.
  - Suspected pneumonitis should be confirmed with radiographic imaging and other infectious and disease-related aetiologies excluded, and managed as recommended in product information.
- **Immune-mediated hepatitis**
  - Immune-mediated hepatitis, defined as requiring the use of systemic corticosteroids and with no clear alternate aetiology, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Monitor alanine aminotransferase, aspartate aminotransferase, total bilirubin, and alkaline phosphatase levels before initiation of treatment and before each subsequent infusion. Additional monitoring is to be considered based on clinical evaluation.
- **Immune-mediated colitis**
  - Immune-mediated colitis or diarrhoea, defined as requiring the use of systemic corticosteroids and with no clear alternate aetiology, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Adverse drug reactions of intestinal perforation and large intestine perforation were reported in patients receiving Imfinzi® in combination with tremelimumab.
  - Patients should be monitored for signs and symptoms of colitis/diarrhoea and intestinal perforation and managed as recommended in product information.
- **Immune-mediated endocrinopathies**
  - Immune-mediated hypothyroidism, hyperthyroidism and thyroiditis occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab, and hypothyroidism may follow hyperthyroidism. Patients should be monitored for abnormal thyroid function tests before and periodically during treatment and as indicated based on clinical evaluation.
  - Immune-mediated adrenal insufficiency occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Patients should be monitored for clinical signs and symptoms of adrenal insufficiency.
  - Immune-mediated type 1 diabetes mellitus, which can first present as diabetic ketoacidosis that can be fatal if not detected early, occurs in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Patients should be monitored for clinical signs and symptoms of type 1 diabetes mellitus.
  - Immune-mediated hypophysitis or hypopituitarism occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Patients should be monitored for clinical signs and symptoms of hypophysitis or hypopituitarism.
- **Immune-mediated nephritis**
  - Immune-mediated nephritis, defined as requiring use of systemic corticosteroids and with no clear alternate aetiology, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Patients should be monitored for abnormal renal function tests prior to and periodically during treatment with Imfinzi® or Imfinzi® in combination with tremelimumab and managed as recommended in product information.
- **Immune-mediated rash**

- Immune-mediated rash or dermatitis (including pemphigoid), defined as requiring use of systemic corticosteroids and with no clear alternate aetiology, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Events of Stevens-Johnson Syndrome or toxic epidermal necrolysis have been reported in patients treated with PD-1 inhibitors. Patients should be monitored for signs and symptoms of rash or dermatitis and managed as recommended in product information.

❖ **Immune-mediated myocarditis**
- Immune-mediated myocarditis, which can be fatal, occurred in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Patients should be monitored for signs and symptoms of immune-mediated myocarditis and managed as recommended in product information.

❖ **Immune-mediated pancreatitis**
- Immune-mediated pancreatitis, occurred in patients receiving Imfinzi® in combination with tremelimumab and chemotherapy. Patients should be monitored for signs and symptoms of immune-mediated pancreatitis and managed as recommended in product information.

❖ **Other immune-mediated adverse reactions**
- Given the mechanism of action of Imfinzi® or Imfinzi® in combination with tremelimumab, other potential immune-mediated adverse reactions may occur. The following immune-related adverse reactions have been observed in patients treated with Imfinzi® monotherapy or Imfinzi® in combination with tremelimumab: myasthenia gravis, myelitis transverse, myositis, polymyositis, meningitis, encephalitis, Guillain-Barré syndrome, immune thrombocytopenia and cystitis noninfective. Patients should be monitored for signs and symptoms and managed as recommended in product information.

❖ **Infusion-related reactions**
- Patients should be monitored for signs and symptoms of infusion-related reactions. Severe infusion-related reactions have been reported in patients receiving Imfinzi® or Imfinzi® in combination with tremelimumab. Infusion-related reactions should be managed as recommended in product information.

❖ **Patients excluded from clinical studies**
- Patients with the following were excluded from clinical studies: a baseline ECOG performance score ≥ 2; active or prior documented autoimmune disease within 2 years of initiation of the study; a history of immunodeficiency; a history of severe immune-mediated adverse reactions; medical conditions that required systemic immunosuppression, except physiological dose of systemic corticosteroids (≤ 10 mg/day prednisone or equivalent); uncontrolled intercurrent illnesses; active tuberculosis or hepatitis B or C or HIV infection or patients receiving live attenuated vaccine within 30 days before or after the start of Imfinzi®.
- In the absence of data, durvalumab should be used with caution in these populations after careful consideration of the potential benefit/risk on an individual basis.
- The safety of concurrent prophylactic cranial irradiation with Imfinzi® in patients with ES-SCLC is unknown.

Study characteristics [8-11]

Trial name	*n*	Intervention (I)[3]	Intervention (I2)	Comparator (C)	PE	Median follow-up	Characteristics	Biomarker	Funding	Publication(s)
HIMALAYA NCT03298451	1,171 (1:1:1)	**STRIDE=** tremelimumab 300mg, one dose + durvalumab 1500mg every 4 weeks	durvalumab 1500mg every 4 weeks	sorafenib 400mg twice daily	OS for STRIDE vs. sorafenib	33.18 vs. 32.56 vs. 32.23 months	**ongoing**[4], global, open-label, phase 3 trial	PD-L1	AstraZeneca	HIMALAYA trial [10]

Inclusion criteria[5]	Exclusion criteria	Patient characteristics at baseline (I vs. I2 vs. C, n=393 vs. n=389 vs. n=389)
❖ Patients ≥18 years; body weight >30 kg; written informed consent and any locally required authorization.	❖ Any unresolved toxicity NCI-CTCAE Grade ≥2 from previous anticancer therapy. ❖ Any concurrent chemotherapy, study drug, or biologic or hormonal therapy for cancer treatment.	❖ Median age: 65.0 (range, 22–86) vs. 64.0 (range, 20–86) vs. 64.0 (range, 18–88) ❖ Male sex: 83.2% vs. 83.0% vs. 86.6% ❖ Region

[3] Originally, there were 4 treatment groups; one group received 75mg of tremelimumab every 4 weeks for four doses plus 1500mg of durvalumab every 4 weeks (a regimen termed T75+D). Data from a preplanned analysis demonstrated that, although all regimens had acceptable side effects and manageable safety profiles, T75+D did not meaningfully differentiate from durvalumab monotherapy in terms of efficacy. Thus, enrolment to T75+D in HIMALAYA was closed.

[4] HIMALAYA trial is currently ongoing; estimated study completion date is 08/2024.

[5] For detailed in- and exclusion criteria, please see trial protocol.

- ❖ Confirmed HCC based on histopathological findings from tumour tissues.
- ❖ Must not have received prior systemic therapy for HCC.
- ❖ Must not be eligible for locoregional therapy for unresectable HCC. For patients who progressed after locoregional therapy for HCC, locoregional therapy must have been completed ≥28 days before the baseline scan for the current study.
- ❖ Barcelona Clinic Liver Cancer (BCLC) stage B (that is not eligible for locoregional therapy) or stage C.
- ❖ Child-Pugh Score class A.
- ❖ ECOG PS of 0 or 1 at enrolment.
- ❖ Patients with HBV infection who are eligible for inclusion must be treated with antiviral therapy to ensure adequate viral suppression before enrolment.
- ❖ Patients with HCV infection must have a confirmed diagnosis of HCV characterized by the presence of detectable HCV RNA or anti-HCV antibody upon enrolment.
- ❖ At least 1 measurable lesion, not previously irradiated, that can be accurately measured at baseline as ≥10 mm in the longest diameter with CT or MRI, and that is suitable for accurate repeated measurements as per RECIST 1.1 guidelines.
- ❖ Adequate organ and marrow function:
  - Haemoglobin ≥9 g/dL
  - Absolute neutrophil count ≥1000/μL
  - Platelet count ≥75000/μL
  - Total bilirubin ≤2.0×ULN
  - AST and ALT ≤5×ULN
  - Albumin ≥2.8 g/dL
  - International normalized ratio ≤1.6
  - Calculated creatinine clearance ≥50 mL/minute as determined by Cockcroft-Gault (using actual body weight) or 24-hour urine creatinine clearance.
- ❖ Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients.

- ❖ Known allergy or hypersensitivity to any of the study drugs or any of the study drug excipients.
- ❖ Radiotherapy treatment to more than 30% of the bone marrow or with a wide field of radiation within 28 days of the first dose of study drug(s).
- ❖ Major surgical procedure within 28 days prior to the first dose of study drug(s).
- ❖ History of allogeneic organ transplantation.
- ❖ History of hepatic encephalopathy within past 12 months or requirement for medications to prevent or control encephalopathy.
- ❖ Ascites that requires ongoing paracentesis, within 6 weeks prior to the first scheduled dose, to control symptoms.
- ❖ Main portal vein thrombosis present on imaging.
- ❖ Active or prior documented GI variceal bleed or history of upper GI bleeding, ulcers, or oesophageal varices with bleeding within 12 months.
- ❖ Patient currently exhibits symptomatic or uncontrolled hypertension defined as diastolic blood pressure >90 mmHg or systolic blood pressure >140 mmHg.
- ❖ Any condition interfering with swallowing pills, uncontrolled diarrhoea, or other contraindication to oral therapy.
- ❖ Active or prior documented autoimmune or inflammatory disorders.
- ❖ Confirmed HBV infection must not be co-infected with HCV or hepatitis D virus.
- ❖ Confirmed HCV infection must not be co-infected with HBV as defined by negative HBsAg.
- ❖ Uncontrolled intercurrent illness as defined in study protocol.
- ❖ History of another primary malignancy.
- ❖ History of leptomeningeal carcinomatosis.
- ❖ Brain metastases or spinal cord compression.
- ❖ Known fibrolamellar HCC, sarcomatoid HCC, or mixed cholangiocarcinoma and HCC.
- ❖ History of active primary immunodeficiency.
- ❖ Active infection including tuberculosis.
- ❖ Current or prior use of immunosuppressive medication within 14 days before the first dose of study drug(s).
- ❖ Receipt of live attenuated vaccine within 30 days prior to the first dose of study drug(s).
- ❖ Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ effective birth control from screening to 90 days after the

  - Asia (excluding Japan): 39.7% vs. 42.9% vs. 40.1%
  - Rest of world (including Japan): 60.3% vs. 57.1% vs. 59.9%
- ❖ ECOG performance status score:
  - 0: 62.1% vs. 60.9% vs. 62.0%
  - 1: 37.7% vs. 38.6% vs. 37.8%
  - 2: 0.3% vs. 0.5% vs. 0.3%
- ❖ Child-Pugh class/score
  - A/5: 75.1% vs. 73.0% vs. 71.2%
  - A/6: 23.4% vs. 24.7% vs. 26.2%
  - B/7: 1.0% vs. 2.1% vs. 2.6%
  - Other: 0.5% vs. 0.3% vs. 0%
- ❖ BCLC stage
  - B: 19.6% vs. 20.6% vs. 17.0%
  - C: 80.4% vs. 79.4% vs. 83.0%
- ❖ Etiology:
  - HBV: 31.0% vs. 30.6% vs. 30.6%
  - HCV: 28.0% vs. 27.5% vs. 26.7%
  - Nonviral: 41.0% vs. 41.9% vs. 42.7%
- ❖ Macrovascular invasion: 26.2% vs. 24.2% vs. 25.7%
- ❖ Extrahepatic spread: 53.2% vs. 54.5% vs. 52.2%
- ❖ AFP ≥400 ng/ml: 36.9% vs. 35.2% vs. 31.9%
- ❖ PD-L1 status:
  - Positive: 37.7% vs. 39.6% vs. 38.0%
  - Negative: 48.1% vs. 48.8% vs. 46.5%
  - Missing: 13.2% vs. 10.8% vs. 11.6%
- ❖ Prior disease-related radiotherapy: 12.2% vs. 8.2% vs. 9.5%

	last dose of durvalumab monotherapy or 180 days after the last dose of durvalumab plus tremelimumab combination therapy. ❖ Patients who have received anti-PD-1, anti PD-L1, or anti CTLA-4 prior to the first dose of study drug(s).	

Efficacy (I2 vs. C)

Noninferiority analysis for durvalumab vs. sorafenib; Data cutoff 27 August 2021

Deaths at data cutoff: 72.0% vs. 75.3%; OS HR 0.86 (95.67% CI, 0.73-1.03)

Because noninferiority was met, the superiority of durvalumab vs. sorafenib was also tested; durvalumab did not demonstrate superiority to sorafenib (p=0.0674).

Median OS: 16.56 months (95% CI, 14.06-19.12) vs. 13.77 months (95% CI, 12.25-16.13)

OS at 36 months: 24.7% vs. 20.2%

Survival rates in the durvalumab arm: 47.4% (95% CI, 42.4-52.3) at 18 months, 39.6% (95% CI, 34.8-44.5) at 24 months and 24.7% (95% CI, 20.0-29.8) at 36 months.

HR for PFS: 1.02 (95% CI, 0.88-1.19)

Patients remaining progression-free at data cutoff: 8.2% vs. 4.9%

Median time to progression: 3.8 months (95% CI, 3.7-5.4) vs. 5.6 months (95% CI, 5.1-5.8)

Confirmed ORR per investigator assessment: 17.0% vs. 5.1%

Confirmed CR: 1.5% vs. 0%

Stable disease: 37.8 vs. 55.5%

Median DoR: 16.8 months vs.18.4 months

Median time to response: 2.09 months vs. 3.78 months

Patients remaining in response at 12 months: 57.8% vs. 63.2%

Safety (I2 vs. C; n=388 vs. n=374)

Treatment-emergent AEs of any cause

- **Any:** 88.9% vs. 95.5%
- **Any serious:** 29.6% vs. 29.7%
- **Any grade 3 or 4:** 37.1% vs. 52.4%
- **Leading to discontinuation:** 8.2% vs. 16.8%
- **Leading to death:** 6.7% vs. 7.2%
- **Immune-mediated requiring high-dose steroids:** 9.5% vs. 1.9%
- **Any grade 3 or 4 immune-mediated:** 6.4% vs. 2.4%
- **Immune-mediated leading to death:** 0% vs. 0%
- **Any grade 3 or 4 hepatic SMQ:** 13.9% vs. 10.4%

Treatment-related AEs

- **Any:** 52.1% vs. 84.8%
- **Any serious:** 8.2% vs. 9.4%
- **Grade 3 or 4:** 12.9% vs. 36.9%
- **Leading to discontinuation:** 4.1% vs. 11.0%
- **Leading to death:** 0% vs. 0.8%[6]
- **Grade 3 or 4 immune-mediated:** 6.2% vs. 2.4%
- **Any immune-mediated leading to death:** 0% vs. 0%
- **Grade 3 or 4 hepatic SMQ:** 5.2% vs. 4.5%

Patient-reported outcomes (I2 vs. C) [10, 12]

- ❖ Across treatment arms, compliance rates for PROs were >77% at baseline and >70% overall.
- ❖ Baseline scores were comparable across treatment arms.
- ❖ The median TTD of patient-reported GHS/QoL: 7.4 months for durvalumab vs. 5.7 months for sorafenib, HR 0.77 (0.62–0.96); p=0.030
- ❖ TTD in fatigue, appetite loss, abdominal pain, PF, and GHS/QoL were significantly longer.

ESMO-MCBS version 1.1 [13]

Scale	Int.	Form	MG ST	MG	HR (95.67% CI)	Score calculation	PM	Toxicity	QoL	AJ	FM
Original	NC	2C	-	-	-	Reduced toxicity or improved QoL (using a validated scale) with evidence for statistical non-inferiority or superiority in PFS/OS	4	-	Significantly improved	-	4
Adapted	NC	2C	-	-	-	Reduced toxicity or improved QoL (using a validated scale) with evidence for statistical non-inferiority or superiority in PFS/OS	4	-	Significantly improved	-	4

Risk of bias (RCT) [14]

[6] Treatment-related AEs leading to death in the sorafenib arm included cerebral hematoma, hepatic failure, and haematuria (all n=1 each).

Adequate generation of randomisation sequence	Adequate allocation concealment	Blinding	Selective outcome reporting unlikely	Other aspects which increase the risk of bias	**Risk of bias**
yes low risk	-	no[7] high risk	unclear[8] unclear risk	yes[9] high risk	unclear

Ongoing trials [15]

NCT number/trial name	Description	Estimated study completion date
NCT03298451/ HIMALAYA	Please see above.	08/2024
NCT05312216	A study on the efficiency and safety of durvalumab plus lenvatinib as first-line treatment for unresectable HCC: an open, single-arm, phase II clinical trial.	06/2024
NCT05844046/ MONTBLANC	Sequential or up-front triple treatment with durvalumab, tremelimumab and bevacizumab for non-resectable HCC, a phase II trial.	12/2026

Available assessments

- In October 2019, NIHR published a Health Technology Briefing "Durvalumab in combination with tremelimumab for unresectable hepatocellular carcinoma – first line" [5].
- NICE suspended carrying out a Single Technology Appraisal of durvalumab for untreated unresectable HCC[10] [16].
- No further assessments were identified via CADTH, ICER and G-BA.

Other aspects and conclusions

- In October 2023, the **CHMP adopted a positive opinion** recommending a change to the terms of the marketing authorisation for Imfinzi®, as monotherapy for the first-line treatment of adults with advanced or unresectable HCC. This indication is **not approved by the FDA**.
- **HIMALAYA (**NCT03298451) is an **ongoing,** global, open-label, **phase 3 trial** evaluating STRIDE and durvalumab monotherapy vs. sorafenib in patients with unresectable HCC who had not been previously treated with systemic therapy. Eligible patients were ≥18 years old with histologically confirmed HCC, had no prior systemic therapy, and were ineligible for locoregional therapy. Patients had BCLC stage B or C, Child-Pugh Score class A, an ECOG PS of 0 or 1, and at least one measurable lesion per RECIST v1.1.14. There is a wide range of exclusion criteria, including clinically meaningful ascites, main portal vein thrombosis, or coinfection with hepatitis B and C viruses.
- The primary endpoint of HIMALAYA is OS for STRIDE vs. sorafenib. **Noninferiority for OS for durvalumab vs. sorafenib was a secondary endpoint**. OS was 16.43 months (95% CI, 14.16-19.58) with STRIDE, 16.56 months (95% CI, 14.06-19.12) with durvalumab, and 13.77 months (95% CI, 12.25-16.13) with sorafenib. OS with durvalumab monotherapy was non-inferior to sorafenib; durvalumab **did not demonstrate superiority** to sorafenib.
- **Patient-reported outcomes** were assessed and showed **improvement**: TTD in fatigue, appetite loss, abdominal pain, PF, and GHS/QoL were **significantly longer**.
- The **original and adapted ESMO-MCBS** were applied and resulted in a final adjusted magnitude of clinical benefit **grade of 4** with both scales.
- Since the HIMALAYA trial is currently ongoing and thus final analysis data is not available, the **risk of bias is considered unclear**. However, the risk **is increased** by the open-label design and the collaboration of the sponsor on trial design, collection, analysis, and interpretation of the data.
- Currently, HIMALAYA is the only ongoing phase 3 trial evaluating the indication assessed in this fact sheet. Two ongoing phase 2 trials, assessing durvalumab in different combinations in patients with untreated HCC, were identified.
- Available **data** for the assessed indication is **rare**. Despite showing a significant improvement in GHS/QoL, durvalumab monotherapy did not demonstrate superiority over sorafenib. Hence, final analysis data from the HIMALAYA trial, and further phase 3 data are required to ensure its benefit for the patients.

First published:11/2023

[7] HIMALAYA is an open-label trial.
[8] HIMALAYA trial is currently ongoing.
[9] Industry-funded. The sponsor provided the trial drugs and collaborated with the steering committee on the trial design, collection, analysis, and interpretation of the data. Editorial assistance was funded by the sponsor.
[10] For information, the company have advised that they are no longer pursuing a Marketing Authorisation Application from the Medicines and Healthcare products Regulatory Agency for this indication. Therefore, NICE has decided to suspend this appraisal from its current work programme. NICE will continue to monitor any development and will update interested parties if the situation changes.

Abbreviations: AE=adverse event, AJ=adjustment, ALK=anaplastic lymphoma kinase, BCLC=Barcelona Clinic Liver Cancer, BTC=biliary tract cancer, C=comparator, CADTH=Canada´s Drug and Health Technology Agency, CHMP=Committee for Medicinal Products for Human Use, CI=confidence interval, CR=complete response, CT=Computed tomography, DOR=duration of response, ECOG PS=Eastern Cooperative Oncology Group Performance Status, EGFR=epidermal growth factor receptor, EMA=European Medicines Agency, ES-SCLC=extensive-stage small cell lung cancer, ESMO-MCBS= European Society of Medical Oncology – Magnitude of Clinical Benefit Scale, FDA=Food and Drug Administration, FM=final magnitude of clinical benefit grade, G-BA=Gemeinsamer Bundesausschuss, GHS=global health status, HBV=Hepatitis B virus, HCC=hepatocellular carcinoma, HCV=Hepatitis C virus, HR=hazard ratio, I=intervention, ICER=Institute for Clinical and Economic Review, ILD=interstitial lung disease, Int.=intention, MG=median gain, MRI=Magnetic resonance imaging n=number of patients, NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Event, NICE=National Institute for Health Care Excellence, NSCLC=non-small cell lung cancer, ORR=objective response rate, OS=overall survival, PD-L1=programmed cell death ligand 1, PE=primary endpoint, PFS=progression-free survival, PM=preliminary grade, QoL=quality of life, RECIST 1.1=Response Evaluation Criteria in Solid Tumours version 1.1, RNA=ribonucleic acid, SAE=serious adverse event, SMQ=Standardized MedDRA Queries, ST=standard treatment, STRIDE=Single Tremelimumab Regular Interval Durvalumab, TTD=time to deterioration, ULN=upper limit of normal

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