Drugs (2022) 82:593–599
https://doi.org/10.1007/s40265-022-01693-4

ADISINSIGHT REPORT

Sugemalimab: First Approval

Sohita Dhillon[1] · **Sean Duggan**[1]

Published online: 17 March 2022

Abstract
Sugemalimab (Cejemly® in China) is a fully human, full length, anti-programmed death ligand 1 (PD-L1) immunoglobulin G4 (IgG4) monoclonal antibody (mAb) that is being developed by CStone Pharmaceuticals for the treatment of advanced solid tumours and lymphoma. In December 2021, sugemalimab was approved in China for the first-line treatment of epidermal growth factor receptor (EGFR) gene mutation and anaplastic lymphoma kinase (ALK) negative metastatic non-small cell lung cancer (NSCLC) administered in combination with pemetrexed and carboplatin for non-squamous NSCLC and in combination with paclitaxel and carboplatin for squamous NSCLC. Sugemalimab is under regulatory review as consolidation treatment in patients with stage III NSCLC in China. Clinical studies assessing sugemalimab for the treatment of several other cancers, including liver cancer, gastric cancer, oesophageal cancer, Hodgkin lymphoma and extranodal natural killer/T cell lymphoma are underway in China, the US and Australia. This article summarizes the milestones in the development of sugemalimab leading to this first approval for the first-line treatment of EGFR gene mutation and ALK-negative metastatic NSCLC.

Digital Features for this AdisInsight Report can be found at https://doi.org/10.6084/m9.figshare.19225272.

Sugemalimab (Cejemly® in China): Key points

A fully human, full-length anti PD-L1 IgG4 mAb being developed by CStone Pharmaceuticals for the treatment of advanced solid tumours and lymphoma

Received its first approval on 21 December 2021 in China

Approved for use as first-line treatment of EGFR gene mutation and ALK negative metastatic NSCLC, given in combination with pemetrexed and carboplatin for non-squamous NSCLC and in combination with paclitaxel and carboplatin for squamous NSCLC

This profile has been extracted and modified from the *AdisInsight* database. *AdisInsight* tracks drug development worldwide through the entire development process, from discovery, through pre-clinical and clinical studies to market launch and beyond.

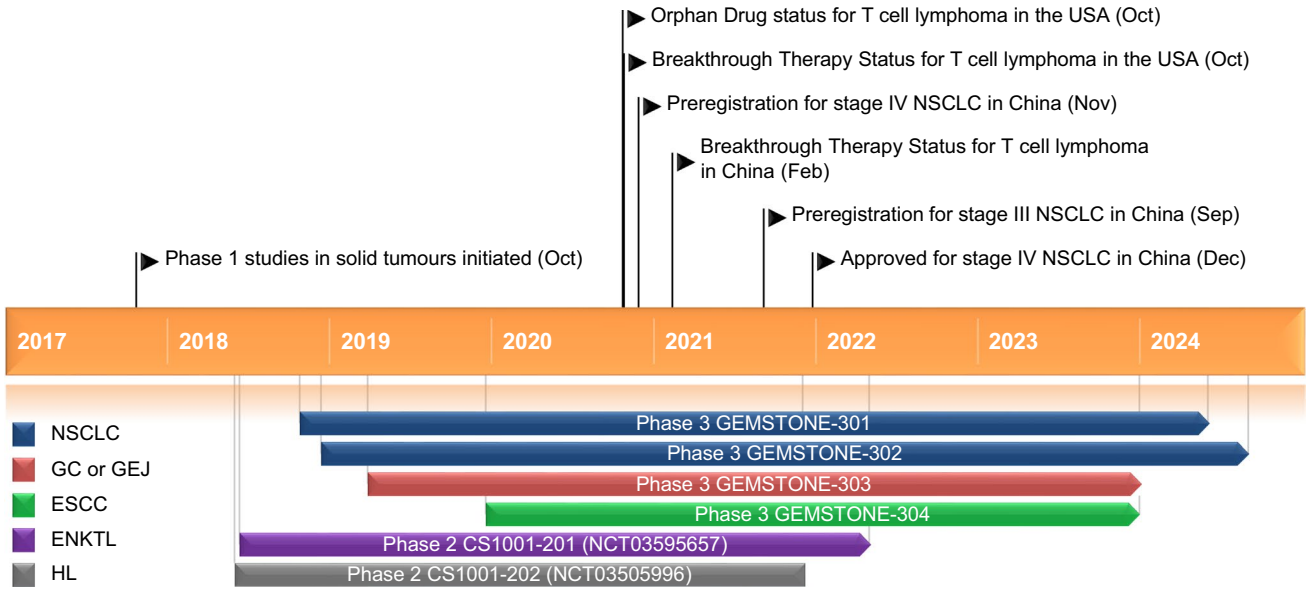
✉ Sohita Dhillon
dru@adis.com

[1] Springer Nature, Mairangi Bay, Private Bag 65901, Auckland 0754, New Zealand

1 Introduction

The emergence of immune checkpoint inhibitors over the last decade or so has revolutionized cancer management. Immune checkpoints are a set of inhibitory and stimulatory pathways that regulate immune responses [1]. Cancer cells evade immune recognition by co-opting certain immune-checkpoint pathways to promote an immunosuppressive state that favours immune evasion and tumour growth. Immune checkpoint inhibitors, such as antibodies targeting the programmed cell death-1 (PD-1)/programmed death-ligand 1 (PD-L1) axis, block the effects of selected inhibitory pathways to augment the host immune system to target tumour cells [1].

Sugemalimab (Cejemly® in China) is a first-in-class, fully human, full length, anti-PD-L1 immunoglobulin G4 (IgG4) monoclonal antibody that is being developed by CStone Pharmaceuticals for the treatment of advanced solid tumours and lymphoma [2–4]. On 21 December 2021 [4], sugemalimab was approved in China for the first-line treatment of epidermal growth factor receptor (EGFR) gene mutation and anaplastic lymphoma kinase (ALK) negative metastatic NSCLC, given in combination with pemetrexed and carboplatin for non-squamous NSCLC and in combination with paclitaxel and carboplatin for squamous NSCLC [3]. The recommended dosage of sugemalimab is 1200 mg administered intravenously over 60 min once every 3 weeks until disease progression or intolerable



Key milestones in the development of sugemalimab for the treatment of non-small cell lung cancer. *ENKTL* extranodal natural killer/ T cell lymphoma, *ESCC* oesophageal squamous cell carcinoma, *GC* gastric adenocarcinoma, *GEJ* gastro-oesophageal junction adenocarcinoma, *HL* Hodgkin lymphoma, *NSCLC* non-small cell lung cancer.

toxicity occurs [3]. Clinical studies assessing sugemalimab for the treatment of several other cancers, including liver cancer, gastric cancer, oesophageal cancer, Hodgkin lymphoma and extranodal natural killer/T cell lymphoma (ENKTL) are underway in China, the US and Australia.

1.1 Company Agreements

In 2018, CStone Pharmaceuticals and IMPACT Therapeutics signed a worldwide clinical collaboration for the evaluation of sugemalimab in combination therapy senaparib monoclonal antibody [Poly(ADP-ribose) polymerase inhibitor] for the treatment of advanced solid tumours [5]. In June 2019, CStone Pharmaceuticals and Bayer entered a global clinical collaboration for the evaluation of sugemalimab in combination with regorafenib (small-molecule multi-kinase inhibitor) for the treatment of multiple cancers, including gastric cancer, with initial focus in China. As per the terms of the collaboration, CStone Pharmaceuticals was to be the study sponsor and Bayer was to provide regorafenib for the clinical trial program [6].

In October 2020, CStone Pharmaceuticals and Pfizer entered into a licensing agreement for the development and commercialization of CStone's sugemalimab in mainland China, and to bring additional oncology assets to the Greater China market [7]. Under the terms of agreement, Pfizer obtained exclusive commercialization rights to sugemalimab in mainland China, while CStone Pharmaceuticals continued to lead clinical development and regulatory strategy for five selected indications [7]. In October 2020, CStone Pharmaceuticals entered into the licensing agreement with EQRx to out-license sugemalimab outside of Greater China. EQRx obtained exclusive rights to lead global development and commercialisation worldwide, excluding Mainland China, Taiwan, Hong Kong and Macau [8, 9].

In October 2021, EQRx entered a long-term, strategic partnership with the National Health Service in England to secure patient access to EQRx's pipeline of innovative cancer medicines, including sugemalimab, contingent on regulatory approval by the UK Medicines and Healthcare products Regulatory Agency (MHRA) and a positive health technology assessment recommendation by NICE [10]. EQRx was granted an Innovation Passport designation for sugemalimab through the Innovative Licensing and Access Pathway (ILAP) from partner organizations including the MHRA, NICE and Scottish Medicines Consortium; the aim of ILAP is to accelerate development and access to promising medicines in the UK, with benefits including the potential for an accelerated Marketing Authorization Application assessment.

2 Scientific Summary

2.1 Pharmacodynamics

Sugemalimab is a high affinity, fully human, full length, anti-PD-L1 IgG4 monoclonal antibody that binds selectively to PD-L1 and blocks its interaction with PD1 and leucocyte differentiation antigen CD80 (B7.1) [2–4]. Sugemalimab is produced by Ligand Pharmaceutical's OmniRat® transgenic animal platform, which can produce

fully human antibodies [4]. Sugemalimab mirrors the natural IgG4 human antibody, which may reduce the risk of immunogenicity and potential toxicities in patients [4].

A receptor occupancy bioanalysis of CD3+ T cells in peripheral blood samples from three patients receiving sugemalimab 10 mg/kg and four patients receiving sugemalimab 1200 mg in a phase 1 study in patients with advanced solid tumours (NCT03744403), showed 100% PD-L1 receptor occupancy prior to sugemalimab administration on day 1 cycle 2 [3]. A crystal structure of the sugemalimab-human PD-L1 complex showed that sugemalimab binds perpendicularly to PD-L1, and its binding epitope overlaps with the human PD-1 binding site [2]. Being an IgG4 antibody, sugemalimab does not activate antibody-dependent cellular toxicity or complement-dependent cytotoxicity to a significant extent [2, 3].

In a mixed lymphocyte reaction, sugemalimab induced the proliferation of CD4+ T lymphocytes and the production of interferon γ and interleukin 2 [2]. In vivo, sugemalimab inhibited tumour growth in a human PD-L1 expressing murine colon carcinoma mouse model [2, 3]. In a dual-humanized PD-1/PD-L1 expressing murine mouse model where human PD-L1 is expressed both in the host and tumour cells, sugemalimab increased the cytotoxic T cell/regulatory T cell ratio, upregulated M1 macrophages and downregulated myeloid-derived suppressor cells. This suggests that sugemalimab may induce a pro-anti-tumour immune response by modulating PD-L1 expressing myeloid cells [2].

2.2 Pharmacokinetics

The pharmacokinetics of sugemalimab were initially assessed in the phase 1a part of a phase 1a/1b study in 29 patients with advanced solid tumours or lymphomas (NCT03312842) [3, 11]. Systemic exposure to intravenously-administered sugemalimab was approximately dose proportional over a dose range of 3 mg/kg to 40 mg/kg ($n = 13$), including a 1200 mg fixed dose ($n = 16$). After a single intravenous 1200 mg dose in 16 patients with advanced solid tumours, mean volume of distribution of sugemalimab was 4.25 L, mean clearance was 0.176 L/day, and mean elimination half-life was 17.56 days [3, 11]. With repeated dosing, sugemalimab steady state was reached after 4 cycles; the accumulation index of area under the concentration-time curve was 2.0 and C_{max} was 1.74 for the 1200 mg dose group [3, 11].

Bodyweight, albumin, sex and tumour type did not affect the pharmacokinetics of sugemalimab to significant extent in a population pharmacokinetic analysis of data from patients with advanced metastatic NSCLC who received first-line treatment with sugemalimab [3]. The elimination rate of sugemalimab decreased over time, with the reduction in rate not considered clinically significant. At steady state, the clearance of sugemalimab in these patients was 0.259 L/day, and the elimination half-life was ~ 20.4 days [3].

Features and properties of sugemalimab

Alternative names	Cejemly; CS1001; WBP 3155
Class	Antineoplastics; immunotherapies; monoclonal antibodies
Mechanism of action	Fully human, full length, anti-PD-L1 IgG4 monoclonal antibody that blocks the interaction of PD-L1 with PD1 and B7.1
Route of administration	Intravenous
Pharmacodynamics	High affinity IgG4 monoclonal antibody that binds selectively to PD-L1
	100% receptor occupancy within the first 3 weeks in patients with advanced solid tumours
	Does not activate antibody-dependent cellular toxicity or complement-dependent cytotoxicity
	Inhibited tumour growth in a human PD-L1 expressing murine colon carcinoma mouse model
Pharmacokinetics	Maximum serum concentration achieved at the end of infusion
	Steady state reached after 4 cycles; accumulation index of AUC 2.0 and of C_{max} 1.74
	In patients with NSCLC, apparent clearance 0.259 L/day; elimination half-life ~ 20.4 days
Adverse events	
Most frequent grade 3/4	Neutrophils, decreased white blood cells, anaemia, decreased platelets, neutropenia
Serious	Anaemia, pneumonia, decreased platelets
ATC codes	
WHO ATC code	L01X-C (monoclonal antibodies)
EphMRA ATC code	L1G (monoclonal Antibody Antineoplastics)

Reported are treatment-related adverse events with sugemalimab plus platinum-based chemotherapy in patients with stage IV metastatic NSCLC

AUC area under the concentration-time curve, *B7.1* leucocyte differentiation antigen CD80, C_{max} peak serum concentration, *PD-1* programmed cell death 1, *PD-L1* programmed death ligand 1, *NSCLC* non-small cell lung cancer

2.3 Therapeutic Trials

2.3.1 Non-Small Cell Lung Cancer

2.3.1.1 Phase 3 GEMSTONE-302 Trial Sugemalimab plus chemotherapy as first-line therapy improved progression-free survival (PFS) to a statistically significant and clinically meaningful extent in patients with previously untreated non-squamous or squamous metastatic NSCLC who were participating in the pivotal, ongoing, double-blind, phase 3 GEMSTONE-302 trial (NCT03789604) [12]. Eligible patients (median age 63 years) with stage IV squamous or non-squamous NSCLC without known EGFR sensitising mutations, or *ALK*, *ROS1* or *RET* fusions and no previous systemic treatment for metastatic disease were randomized to receive intravenous sugemalimab 1200 mg once every 3 weeks [intent-to-treat (ITT) $n = 320$] or placebo (ITT $n = 159$), plus platinum-based chemotherapy (carboplatin plus paclitaxel for squamous NSCLC, and carboplatin plus pemetrexed for non-squamous NSCLC) for ≤ 4 cycles. This was followed by maintenance therapy with sugemalimab or placebo for squamous NSCLC, and sugemalimab or placebo plus pemetrexed for non-squamous NSCLC for up to 2 years (35 cycles) or until disease progression or unacceptable toxicity.

The study met its primary endpoint at the prespecified interim PFS analysis (median follow-up 8.6 months), with significantly longer investigator-assessed PFS in patients receiving sugemalimab compared with those receiving placebo (median PFS 7.8 vs 4.9 months; stratified hazard ratio (HR) 0·50; 95% CI 0.39–0.64; $p < 0·0001$) [12]. The PFS benefit observed with sugemalimab was sustained at the prespecified final PFS analysis (median follow-up 17.8 months), with significantly longer PFS in the sugemalimab group than in the placebo group (median 9.0 vs 4.9 months; stratified HR 0·48; 95% CI 0.39–0.60; $p < 0.0001$). In subgroup analyses, improvement in PFS was observed with sugemalimab versus placebo both in patients with squamous (median 8.3 vs 4.8 months; unstratified HR 0.34; 95% CI 0.24–0.48) and in those with non-squamous (median 9.6 vs 5.9 months; unstratified HR 0.59; 95% CI 0.45–0.79) NSCLC. In a post hoc analysis, PFS benefit with sugemalimab versus placebo was observed regardless of PD-L1 expression both in the squamous and non-squamous subgroups [12].

A preliminary overall survival (OS) analysis at the time of final PFS analysis suggested an OS benefit with sugemalimab versus placebo (median OS 22.8 vs 17.7 months; stratified HR 0.67 (95% CI 0.50–0.90), $p = 0·0064$); the 12-month OS rate was 72.4% versus 62.0% and the 24-month rate was 47.1% versus 38.1% in the sugemalimab and placebo groups [12]. The objective response rate (ORR) was 63.4% with sugemalimab versus 40.3% with placebo, and the median duration of response (DoR) was 9.8 versus 4.4 months, respectively [12].

2.3.1.2 Phase 3 GEMSTONE-301 Interim results of the ongoing, double-blind, phase 3 GEMSTONE-301 trial (NCT03728556) indicate that consolidation therapy with sugemalimab could be effective consolidation therapy in patients with locally advanced, unresectable, stage III NSCLC who have not progressed after concurrent or sequential chemoradiotherapy (CRT) [13]. Patients (median age 61 years) were randomized to receive sugemalimab 1200 mg once every 3 weeks (ITT $n = 255$) or placebo (ITT $n = 126$) for up to 2 years or until disease progression or unacceptable toxicity. At a prespecified interim PFS analysis (median follow-up 14.3 and 13.7 months in the sugemalimab and placebo groups), the blinded independent central review (BICR)-assessed PFS (primary endpoint) was significantly longer with sugemalimab versus placebo (median 9.0 vs 5.8 months; stratified HR 0.64; 95% CI 0.48–0.85; $p = 0.0026$). Prespecified subgroup analyses showed that PFS was improved both in patients with prior concurrent (median PFS 10.5 vs 6.4 months; unstratified HR 0.66; 95% CI 0.44–0.99) and prior sequential (median PFS 8.1 vs 4.1 months; unstratified HR 0.59; 95% CI 0.39–0.91) CRT. BICR-assessed ORRs did not differ significantly between the sugemalimab and placebo groups (20.6% vs 19.4%). The median DoR was not reached in the sugemalimab group and was 6.0 months in the placebo group. OS data, although immature, appeared to favour sugemalimab (median not reached vs 24.1 months; HR 0.44; 95% CI 0.27–0.73; $p = 0.0009$) [13].

2.3.2 Extranodal Natural Killer/T Cell Lymphoma

Sugemalimab monotherapy demonstrated anti-tumour activity in patients with relapsed or refractory ENKTL according to preliminary results from the ongoing, multicentre, single-arm, phase 2, CS1001-201 study (NCT03595657) [14]. Patients (median age 44 years) who had relapsed or refractory disease after prior asparaginase-based chemotherapy or chemoradiotherapy received sugemalimab 1200 mg once every 3 weeks up to 2 years or until disease progression or unacceptable toxicity. After a median follow-up of 5.55 months, the investigator-assessed ORR (primary endpoint) in the efficacy evaluable population ($n = 22$) was 40.9% (9/22), with seven (31.8%) complete responses (CRs) and two (9.1%) partial responses; in addition, one patient had PR after pseudo-progression. The median DoR was not reached. In updated data, three additional patients achieved objective response, resulting in an ORR of 44% (11/25) and a CR rate of 36% [14].

2.3.3 Solid Tumours or Lymphomas

Evidence of anti-tumour activity with sugemalimab was observed in an ongoing, phase 1a/1b dose-escalation and -expansion study (NCT03312842) in patients with advanced

solid tumours or lymphomas [11]. Twenty-nine patients (median age 53 years) in phase 1a received sugemalimab 3–40 mg/kg in four cohorts ($n = 3$ or 4 per group) or sugemalimab 1200 mg fixed dose ($n = 16$) once every 3 weeks. The median duration of treatment across all cohorts was 126 days. No disease limiting toxicities were observed at any dose level and the maximum tolerated dose was not reached; sugemalimab 1200 mg once every 3 weeks was determined to be the recommended phase 2 dose (RP2D; primary endpoint). The ORR was 24.1%, with seven PRs; the median DoR and PFS were 13.7 and 4.8 months, respectively, and the median OS was not reached.

In phase 1b of the study, 178 patients were enrolled. Of these, 69 patients (median age 55 years) received sugemalimab (RP2D) as monotherapy, including patients with cholangiocarcinoma/gallbladder carcinoma (CC/GBC; $n = 29$), hepatocellular carcinoma (HCC; $n = 19$) and high-microsatellite instability or mismatch repair gene deficient phenotype (MSI-H/dMMR; $n = 21$) [11]. Sugemalimab (R2PD) in combination with standard of care chemotherapy was administered to 109 patients (median age 60 years), including patients with gastric adenocarcinoma or gastroesophageal junction adenocarcinoma (GAC/GEJAC; $n = 29$), ESCC ($n = 39$), non-squamous NSCLC ($n = 21$) and squamous NSCLC ($n = 20$). The primary endpoint was investigator-assessed ORR. Across the sugemalimab monotherapy cohorts, 12 of 69 patients achieved PRs; in the CC/GBC, HCC and MSI-H/dMMR cohorts the ORRs achieved were 6.9%, 10.5% and 38.1%, respectively. In the sugemalimab combination therapy cohorts, 68 of 107 evaluable patients had PRs; in the GA/GAGC, ESCC, non-squamous NSCLC and Squamous NSCLC cohorts the ORRs achieved were 62.1%, 67.6%, 47.6% and 75.0%, respectively.

2.4 Adverse Events

2.4.1 NSCLC

2.4.1.1 Phase 3 GEMSTONE-302 Sugemalimab plus platinum-based chemotherapy was generally well tolerated in patients with metastatic squamous or non-squamous NSCLC who were participating in the pivotal, double-blind, phase 3 GEMSTONE-302 trial (NCT03789604) [12]. The addition of sugemalimab did not appear to increase the incidence of adverse events (AEs) commonly associated with chemotherapy, and no unexpected safety signals were observed.

Treatment-related AEs occurred in 99% (317/320) of patients in the sugemalimab group and 96% (153/159) of patients in the placebo group, with grade 3 or 4 AEs reported in 54% and 56% of patients, respectively [12]. The most common treatment-related grade 3 or 4 AEs with sugemalimab and placebo were decreased neutrophils (33% vs 33%), decreased white blood cells (14% vs 17%), anaemia (13% vs 11%), decreased platelets (10% vs 9%) and neutropenia (4% vs 4%). Treatment-related serious AEs were reported in 23% of patients receiving sugemalimab and 20% of patients receiving placebo, with the most common AEs being anaemia (3% vs 3%), pneumonia (3% vs 4%) and decreased platelets (3% vs 3%) [12].

Treatment-related AEs resulted in discontinuation of treatment in 14% of sugemalimab and 9% of placebo recipients, with anaemia (2% vs 2%), pneumonia (2% vs 2%) and abnormal hepatic function (1% vs 1%) being the most common causes of treatment discontinuation [12]. Chemotherapy dose reduction was required in 14% of patients in the sugemalimab group and 18% of patients in the placebo

Key clinical trials of sugemalimab sponsored by CStone Pharmaceuticals

Drug(s)	Indication	Phase	Status	Location(s)	Identifier
Sugemalimab, placebo	NSCLC	3	Ongoing	China	NCT03728556; GEMSTONE-301; CS1001-301; CTR20181429
Sugemalimab, carboplatin, pemetrexed, placebo	NSCLC	3	Ongoing	China	NCT03789604; GEMSTONE-302; CS1001-302
Sugemalimab, placebo, oxaliplatin, capecitabine	GC or GEJ	3	Ongoing	China	NCT03802591; GEMSTONE-303; CS1001-303
Sugemalimab, placebo, fluorouracil, cisplatin	ESCC	3	Ongoing	China	NCT04187352; GEMSTONE-304; CS1001-304
Sugemalimab	EKNTL	2	Ongoing	China, USA	NCT03595657; CS1001-201; CTR20180519
Sugemalimab	Hodgkin lymphoma	2	Ongoing	China	NCT03505996; CS1001-202; CTR20180423
Sugemalimab, regorafenib	Solid tumours	1b/2	Ongoing	Australia	NCT04200404; CS1001/ regorafenib-101
Sugemalimab, fisogatinib	HCC	1b/2	Ongoing	China	NCT04194801; CS3008-101

EKNTL extranodal natural killer/ T cell lymphoma, *ESCC* oesophageal squamous cell carcinoma, *GC* gastric adenocarcinoma, *GEJ* gastro-oesophageal junction adenocarcinoma, *HCC* hepatocellular carcinoma, *NSCLC* non-small cell lung cancer

group. Fatal AEs occurred in 10 (3%) sugemalimab recipients, including pneumonia ($n = 2$), pneumonia with respiratory failure, myelosuppression with septic shock, respiratory failure, abdominal pain, cardiac failure and immune-mediated pneumonitis ($n = 1$ each), and unspecified causes ($n = 2$); fatal AEs occurred in 2 (1%) placebo recipients (pneumonia and multiple organ dysfunction syndrome) [12].

Immune-related treatment-emergent AEs (AEs of special interest) occurred in 25% of patients in the sugemalimab group (vs 3% in the placebo group), most of which were of mild or moderate severity and consistent with those expected for the drug class. The most common immune-related treatment-emergent AEs with sugemalimab were hypothyroidism (11% vs 1%), hyperthyroidism (7% vs 1%) and non-severe skin adverse reactions (7% vs 1%) [12].

2.4.1.2 Phase 3 GEMSTONE-301 In the phase 3 GEMSTONE-301 study (NCT03728556), the safety profile of sugemalimab as consolidation therapy in patients with locally advanced, unresectable, stage III NSCLC who had not progressed after concurrent or sequential CRT was consistent with that reported previously with sugemalimab monotherapy, with no new safety signals observed [13]. Treatment-emergent AEs occurred in 76% (193/255) of sugemalimab and 58% (73/126) of placebo recipients. Treatment-related grade 3 or 4 AEs were reported in 9% of patients in the sugemalimab and 6% of patients in the placebo group, with the most frequent AE being pneumonitis or immune-mediated pneumonitis (3% vs 1%). Treatment-related serious AEs occurred in 15% and 10% of patients in the sugemalimab and placebo groups, respectively, with pneumonitis or immune-mediated pneumonitis (9% vs 7%), pneumonia (2% vs < 1%) and interstitial lung disease (2% vs 2%) occurring most frequently. Four treatment-related deaths were reported with sugemalimab (pneumonia in two patients, pneumonia with immune-mediated pneumonitis in one patient, and acute hepatic failure in one patient) [13].

Treatment-related AEs resulted in discontinuation of therapy in 9% of sugemalimab and 3% of placebo recipients, with pneumonitis or immune-mediated pneumonitis (2% vs 2%), pneumonia (1% vs <1%) and interstitial lung disease (<1% vs 0) being the most common reasons for treatment discontinuation [13]. AEs of special interest were reported in 43% of sugemalimab and 13% of placebo recipients, with grade 3 or 4 AEs occurring in 4% and 1% of patients, respectively. The most common grade 3 or 4 AE of special interest was pneumonia [13].

2.4.2 Extranodal Natural Killer/T Cell Lymphoma

Sugemalimab was generally well tolerated in patients with relapsed or refractory ENKTL ($n = 29$) participating in the phase 2, CS1001-201 study (NCT03595657) [14]. Over a median treatment duration of 11.7 weeks, treatment-emergent AEs with sugemalimab were reported in 86.2% of patients, with most (74.2%) AEs considered treatment related. The most common treatment-related AEs were pyrexia (20.7%), increased blood thyroid stimulating hormone (13.8%), decreased white blood cells (13.8%) and rash (10.3%). Grade ≥ 3 treatment-related AEs occurred in three (10.3%) patients. Serious AEs were reported in 17.2% of patients, of which one AE (sinus node dysfunction) was considered treatment related. Immune-related AEs occurred in five patients, with one AE of grade 3 severity (rash) and four AEs of grade 1 severity. No death or permanent discontinuation of treatment was considered treatment related [14].

2.4.3 Solid Tumours or Lymphomas

An earlier phase 1a/1b study (NCT03312842) in patients with advanced solid tumours or lymphomas showed that the tolerability profile of sugemalimab as monotherapy or combination therapy with standard of care regimens was generally consistent with that of other anti-PD-L1/anti PD1 monoclonal antibodies [11]. Most AEs in phase 1a and phase 1b of the study were of mild or moderate severity and generally manageable. Treatment-related AEs occurred in 84.1% (58/69) of patients in sugemalimab monotherapy cohorts (15.9% of grade 3–5) and in 92.7% (101/109) of patients in sugemalimab in combination with chemotherapy cohorts (40.4% of grade 3–5).

AEs resulted in the withdrawal of sugemalimab in 7.2% (5/69) and 11.9% (13/109) patients in monotherapy and combination therapy cohorts, respectively [11]. No sugemalimab monotherapy-related fatal AEs were reported. Two fatal AEs (death and cerebral haemorrhage) considered related to sugemalimab and/or chemotherapy were reported in two patients the sugemalimab combination therapy cohort, which occurred when they were treated outside the research centres. Therefore, the relation of these AEs to sugemalimab could not be confirmed [11].

2.5 Ongoing Clinical Trials

In addition to the ongoing studies discussed in Sect. 2.3, the randomized, double-blind, phase 3 GEMSTONE-303 (NCT03802591) has recruited ~ 480 patients to assess the efficacy and safety of sugemalimab plus chemotherapy (oxaliplatin and capecitabine) in patients with gastric adenocarcinoma or gastro-oesophageal junction adenocarcinoma. The primary endpoint of the study is investigator-assessed PFS and OS. Recruitment has also been completed for the randomized, double-blind, phase 3 GEMSTONE-304 study (NCT04187352) that aims to assess the efficacy and safety of sugemalimab plus chemotherapy (fluorouracil and cisplatin) in ~ 420 patients with unresectable locally advanced,

recurrent or metastatic ESCC [15]. The primary endpoints of the study are PFS as assessed by BICR and OS [15].

A single-arm, phase 2 study (NCT03505996) is underway to evaluate the efficacy and safety of sugemalimab monotherapy in 80 patients with relapsed or refractory classical Hodgkin lymphoma. The primary endpoint of the study is ORR. An open-label phase 1b/2 study (NCT04194801) is recruiting ~ 52 patients to assess the efficacy, safety and pharmacokinetics of sugemalimab plus fisogatinib (human fibroblast growth factor receptor 4 inhibitor) in ~ 52 patients with locally advanced or metastatic HCC. The primary outcome measures are the incidence of dose limiting toxicities in phase 1b and ORR in phase 2 of the study.

3 Current Status

Sugemalimab received its first approval in China on 21 December 2021 for the first-line treatment of EGFR gene mutation and ALK negative metastatic NSCLC, given in combination with pemetrexed and carboplatin for non-squamous NSCLC and in combination with paclitaxel and carboplatin for squamous NSCLC [3].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40265-022-01693-4.

Declarations

Funding The preparation of this review was not supported by any external funding.

Authorship and conflict of interest During the peer review process the Manufacturer of the agent under review was offered an opportunity to comment on the article. Changes resulting from any comments received were made by the authors on the basis of scientific completeness and accuracy. Sohita Dhillon is a contracted employee of Adis International Ltd/Springer Nature and Sean Duggan is a salaried employee of Adis International Ltd/Springer Nature and declare no relevant conflicts of interest. All authors contributed to the review and are responsible for the article content.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability Not applicable.

References

1. Marin-Acevedo JA, Kimbrough EO, Lou Y. Next generation of immune checkpoint inhibitors and beyond. J Hematol Oncol. 2021;14(1):45.
2. Zhang J, Li Z, Tang L, et al. The preclinical characterization of CS1001, an anti-PD-L1 IgG4 monoclonal antibody and its activity beyond T cell regulation [abstract]. Cancer Res. 2020;80(16 Suppl):3260.
3. CStone Pharmaceuticals. Sugemalimab: Chinese prescribing information. Suzhou Industrial Park: CStone Pharmaceuticals; 2021.
4. Ligand Pharmaceuticals. Ligand's partner CStone Pharmaceuticals receives approval in China for sugemalimab (Cejemly®) for the first-line treatment of advanced non-small cell lung cancer in combination with chemotherapy [media release]. 22 Dec 2021. https://investor.ligand.com/press-releases/detail/457/ligands-partner-cstone-pharmaceuticals-receives-approval.
5. CStone Pharmaceuticals, Impact Therapeutics. CStone and IMPACT Therapeutics' clinical collaboration progresses to IND filing acceptance for CS1001+IMP4297 combination therapy [media release]. 2 Feb 2019. https://www.cstonepharma.com/en/html/news/2040.html.
6. CStone Pharmaceuticals, Bayer. CStone and Bayer announce global collaboration to evaluate PD-L1 monoclonal antibody CS1001 in combination with regorafenib [media release]. 10 Jun 2019. https://www.cstonepharma.com/en/html/news/2123.html.
7. CStone Pharmaceuticals, Pfizer. CStone, Pfizer enter into strategic collaboration to address oncological needs in China [media release]. 30 Sep 2020. https://www.cstonepharma.com/en/html/news/2463.html.
8. C. Stone Pharmaceuticals. CStone and EQRx enter global strategic partnership for two immune checkpoint inhibitors: sugemalimab (anti-PD-L1) and CS1003 (anti-PD-1) [media release]. 2 Feb 2020. https://www.cstonepharma.com/en/html/news/2486.html.
9. CStone Pharmaceuticals. CStone Pharmaceuticals and EQRx's global strategic cooperation passed the waiting period of the US HSR Act ahead of schedule, and the agreement came into effect [media release]. 20 Nov 2020. https://www.cstonepharma.com/en/uploads/2020/11/200804482673.pdf.
10. EQRx. EQRx and NHSE sign Memorandum of Understanding to enter into England's first population health partnership for cancer drugs [media release]. 19 Oct 2021. https://www.eqrx.com/press-release/eqrx-and-nhse-sign-memorandum-of-understanding-to-enter-into-englands-first-population-health-partnership-for-cancer-drugs/.
11. Gong J, Cao J, Zhang Q, et al. Safety, antitumor activity and biomarkers of sugemalimab in Chinese patients with advanced solid tumors or lymphomas: results from the first-in-human phase 1 trial. Cancer Immunol Immunother. 2022. https://doi.org/10.1007/s00262-021-03102-3.
12. Zhou C, Wang Z, Sun Y, et al. Sugemalimab versus placebo, in combination with platinum-based chemotherapy, as first-line treatment of metastatic non-small-cell lung cancer (GEMSTONE-302): interim and final analyses of a double-blind, randomised, phase 3 clinical trial. Lancet Oncol. 2022. https://doi.org/10.1016/S1470-2045(21)00650-1.
13. Zhou Q, Chen M, Jiang O, et al. Sugemalimab versus placebo after concurrent or sequential chemoradiotherapy in patients with locally advanced, unresectable, stage III non-small-cell lung cancer in China (GEMSTONE-301): interim results of a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol. 2022. https://doi.org/10.1016/s1470-2045(21)00630-6.
14. Huang HQ, Tao R, Zou L, et al. Preliminary results from a multicenter, single-arm, phase 2 study of CS1001, an anti-programmed death-ligand 1 (PD-L1) human monoclonal antibody (mAb), in patients (pts) with relapsed or refractory extranodal natural killer/T cell lymphoma (rr-ENKTL) [abstract]. Blood. 2019;134(Suppl 1):2833.
15. Li J, Bai Y, Li Q, et al. CS1001-304: A phase III study of fluorouracil and cisplatin (FP) with CS1001, an anti-PD-L1 antibody, or placebo in unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) [abstract no. TPS255]. J Clin Oncol. 2021;39(3 Suppl).