

Positive Quality intervention: Cemiplimab-rwlc (Libtayo®) Patient Management

Description: The purpose of this PQI is to discuss the option of using cemiplimab-rwlc for patients with:

1. Locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) previously treated with a hedgehog pathway inhibitor (HHI) or for whom an HHI is not appropriate.
2. Locally advanced or metastatic cutaneous squamous cell carcinoma (laCSCC or mCSCC) who are not candidates for curative surgery or curative radiation.
3. Locally advanced non-small cell lung cancer (NSCLC) where patients are not candidates for surgical resection or definitive chemoradiation or metastatic NSCLC whose tumors have high PD-L1 expression [$\geq 50\%$] as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations.

Background: Cemiplimab is a programmed death receptor-1 (PD-1) monoclonal antibody which acts to block the PD-L1/PD-L2 pathway thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions.¹ Cemiplimab is indicated in treatment of patients with mCSCC or laCSCC who are not candidates for curative surgery or curative radiation. Its efficacy and safety in the treatment of mCSCC and laCSCC was demonstrated in two open-label, multi-center, non-randomized, multicohort studies: Study 1423 and Study 1540. Cemiplimab showed beneficial effect regarding objective response rate (ORR) and duration of response (DOR). In Study 1540, the combined cohort of patients with laCSCC or mCSCC had an ORR of 46% (95% CI, 37-55) and the percentage of patients that had DOR longer than 12 months was 76 % in the mCSCC and 35 % in the laCSCC cohort of patients, respectively.¹

Cemiplimab is also indicated in the treatment of laBCC and mBCC previously treated with a HHI, or for whom a HHI is not appropriate. Although the mBCC indication has accelerated approval status in the USA, it has been granted regular approval for this indication in the European Union.^{1,2} An open-label, multi-center, non-randomized single arm study (Study 1620) showed beneficial effect of cemiplimab in the afore mentioned population. Patients with laBCC had an ORR of 29% (95% CI, 19-40) and the mBCC cohort of patients had an ORR of 21% (95% CI, 8-41). DOR longer than 6 months was present in 100% of mBCC patients and 79.2% of laBCC patients.¹

In addition cemiplimab is indicated in treatment of NSCLC patients with high expression of PD-L1 (Tumor Proportion Score $\geq 50\%$). A randomized, open-label, multi-center study (Study 1624) was conducted which included patients with locally advanced NSCLC who were not candidates for definitive chemoradiation or surgical resection as well as patients with metastatic NSCLC which showed a beneficial effect with cemiplimab.^{1,3} Patients included in this trial did not have EGFR, ALK or ROS1 aberrations. Patients were randomly assigned to treatment with cemiplimab or platinum doublet chemotherapy. The primary efficacy endpoints were overall survival (OS) and progression-free survival (PFS). This study demonstrated a median survival of 22.1 months (95% CI, 17.7- NE) in the group receiving cemiplimab versus 14.4 months (95% CI 11.7, 19.2) in the group receiving chemotherapy. The hazard ratio for PFS was 0.59 (95% CI, 0.49-0.72) and for the OS it was 0.68 (95% CI, 0.53-0.87).¹ In all afore mentioned trials, cemiplimab was used as monotherapy and grade 3 or 4 adverse events were present in the BCC (48%), NSCLC (28%) and in the CSCC (45.2%) patient populations. A substantial proportion of adverse effects were immune-mediated adverse reactions.³⁻⁶

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PQI Process: Upon order of Cemiplimab:¹

- Verify dosing of cemiplimab as an intravenous infusion over 30 minutes
- The recommended dose is 350 mg cemiplimab every 3 weeks for all indications. Administer through an intravenous line containing a sterile, in-line or add-on 0.2-micron to 5-micron filter. Other medicinal products should not be co-administered through the same infusion line
- Withdraw 7 mL (350 mg) from a vial and dilute with 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 1 mg/mL to 20 mg/mL
- Gently mix the solution without shaking
- Cemiplimab injection is a clear to slightly opalescent, colorless to pale yellow solution that may contain trace amounts of translucent to white particles
- Cemiplimab comes in single-dose vial containing 350 mg of cemiplimab in 7 mL of solution
- Cemiplimab should be stored in a refrigerator at 2°C to 8°C (36°F to 46°F)
- When cemiplimab requires interruption or discontinuation for suspected or proven immune-mediated toxicities, consider systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less (*see Table 1*). If patients experience improvement in symptoms to Grade 1 or less, continuously decrease dose of corticosteroids over at least 1 month. In situations when immune-mediated adverse reactions are not controlled with corticosteroids other systemic immunosuppressants can be considered.¹
- Management of a grade 1-2 infusion reaction includes interrupting or slowing the rate of infusion. Cemiplimab should be permanently discontinued for a grade 3-4 infusion reaction and supportive care should be initiated¹

Patient Centered Activities:

- Counsel patient regarding immune-related adverse events and infusion-related reactions
- Consider initiation of steroids as necessary
- Monitor patient for laboratory changes associated with common adverse reactions
- Educate regarding the importance of keeping lab appointments
- Instruct patient to inform provider of any new medications
- Educate when to call the provider
- Patient support available at <https://www.libtayo.com/cscclibtayo-surround>

References:

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2. European Medicines Agency, *Summary of Product Characteristics (SmPC)* cemiplimab-rwlc (LIBTAYO). European Medicines Agency 2021. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002782/WC500168528.pdf. Accessed October 04, 2021.
3. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021;397(10274): 592-604.
4. Rischin D, Migden MR, Lim AM, et al. Phase 2 study of cemiplimab in patients with metastatic cutaneous squamous cell carcinoma: primary analysis of fixed-dosing, long-term outcome of weight-based dosing. *J Immunother Cancer*. 2020;8(1): e000775.
5. Migden MR, Rischin D, Schmuits CD, et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. *N Engl J Med*. 2018;379(4): 341-351.
6. Stratigos AJ, Sekulic A, Peris K, et al. Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy: an open-label, multi-centre, single-arm, phase 2 trial. *Lancet Oncol*. 2021;22(6): 848-857.

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Supplemental Section:

Table 1. Cemiplimab Adverse Reaction Management¹

Immune Mediated Adverse Reaction	Withhold^a Cemiplimab	Permanently Discontinue Cemiplimab
Pneumonitis	Grade 2	Grade 3 or 4
Colitis	Grade 2 or 3	Grade 4
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times ULN or Total bilirubin increases to more than 1.5 and up to 3 times the ULN	AST or ALT increases to more than 8 times the ULN or Total bilirubin increases to more than 3 times the ULN
Hepatitis with tumor involvement of the liver ^b	Baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN
Endocrinopathies (Adrenal insufficiency, hypophysitis, thyroiditis, hypo/hyperthyroidism, Diabetic ketoacidosis)	Grades 3 or 4 ^c	Permanently discontinue depending on severity.
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Grade 4 increased blood creatinine
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Confirmed SJS, TEN, or DRESS
Myocarditis		Grade 2, 3 or 4
Neurological Toxicities	Grade 2	Grades 3 or 4

ALT=alanine aminotransferase, AST=aspartate aminotransferase, DRESS=Drug Rash with Eosinophilia and Systemic Symptoms, SJS=Stevens-Johnson Syndrome, TEN=toxic epidermal necrolysis, ULN=upper limit of normal

a - Resume if partial or complete resolutions of symptoms (Grade 0 - 1) after use of corticosteroids. Cemiplimab should be permanently discontinued in patients that do not have complete or partial resolution of symptoms within 12 weeks of corticosteroid therapy or inability to decrease dose of prednisone (or equivalent) below 10 mg per day after 12 weeks of use

b - If AST and ALT are ≤ to ULN at baseline, withhold or permanently discontinue cemiplimab based on recommendations for hepatitis with no liver involvement

c - Withhold until clinically stable or permanently discontinue depending on severity

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