

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 [$\geq 50\%$], 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. 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% 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% and the mBCC cohort of patients had an ORR of 21%. 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 in the group receiving cemiplimab versus 14.4 months in the group receiving chemotherapy. The hazard ratio for PFS was 0.59 and for the OS it was 0.68.¹ 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

PQI Process: Upon order of Cemiplimab:^{1,2}

- Dose of 350 mg cemiplimab infused over 30 minutes, 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 single dose vial and dilute with 0.9% Sodium Chloride Injection, or 5% Dextrose, to a final concentration between 1 mg/mL-20 mg/mL
- Gently mix the solution without shaking
- Solution will appear clear to slightly opalescent, colorless to pale yellow and may contain trace amounts of translucent to white particles

Important Notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. *Updated 3.8.22*



- Cemiplimab should be stored in a refrigerator at 2°C to 8°C (36°F to 46°F)
- If interruption or discontinuation for suspected/proven immune-mediated toxicities, consider corticosteroid (1-2 mg/kg/day prednisone) until ≤ Grade 1 (Table 1), then taper over 1 month
 - When not controlled with corticosteroids other systemic immunosuppressants can be considered¹
- Management of a grade 1-2 infusion reaction includes interrupting or slowing the rate of infusion; permanently discontinue 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
- Educate regarding the importance of keeping lab appointments
- Instruct patient to inform provider of any new medications
- Educate when to call the provider
- Patient Assistance: [NCODA Financial Assistance Tool](#)

References:

1. LIBTAYO® (cemiplimab-rwlc) [prescribing information].
2. European Medicines Agency. Summary of Product Characteristics (SmPC) cemiplimab-rwlc (LIBTAYO). European Medicines Agency.
3. Sezer A, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50. *Lancet*. 2021;397(10274): 592-604.
4. Rischin D, et al. Phase 2 study of cemiplimab in patients with metastatic cutaneous squamous cell carcinoma. *J Immunother Cancer*. 2020;8(1): e000775.
5. Migden MR, 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, et al. Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy. *Lancet Oncol*. 2021;22(6): 848-857.

Supplemental Section:

Table 1. Cemiplimab Adverse Reaction Management¹

Adverse Reaction	Hold ^a	Permanently Discontinue
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 > 3-8 times ULN or Total bilirubin > 1.5-3 times ULN	AST or ALT > 8 times ULN or Total bilirubin > 3 times ULN
Hepatitis with tumor involvement of the liver ^b	Baseline AST or ALT > 1-3 times ULN and increases > 5-10 times ULN or Baseline AST or ALT > 3-5 times ULN and > 8-10 times ULN	AST or ALT > 10 times ULN or Total bilirubin > 3 times ULN
Endocrinopathies (adrenal insufficiency, hypophysitis, thyroiditis, hypo/hyperthyroidism, diabetic ketoacidosis)	Grades 3 or 4 ^c	Permanently discontinue based 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

Important Notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. Updated 3.8.22