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US Expert Medical Opinion, Inc. 1625 SE, 3rd Avenue Suite 723. Fort Lauderdale, FL 33316. USA

Date November 16th, 2020

Reference: Mr

DOB:

Dear

The following is a report prepared for Mr. based upon my review of the available medical records provided in your MyUSADr. Medical opinion request.

Source of information: Clinical node (doc), lab (doc)

This is a 58-year-old patient with stage IV lung cancer with liver metastases. The information is obtained from patient brief clinical notes and laboratory data provided on November 10, 2020. In summary, the patient essentially had liver ultrasound which revealed a liver lesion, discussed follow-up by an unenhanced CT scan which showed a liver space-occupying lesion. Again based on the clinical notes provided, the patient had no nausea, vomiting, abdominal pain, bloating. Abdominal examination was unremarkable. The patient blood work performed on October 9, 2020 reveals WBC 5.66 hemoglobin 14.7 platelet count 164. Patient's direct bili was 2.31 mmol/L AST 23.65 ALT 14.60 creatinine 94.31 with no reference ranges provided. Work-up also revealed a positive hepatitis B surface antigen, positive hepatitis B surface antibody. The patient CT scanning on October 17, 2020 revealed an upper left lung nodule; there were also 2 lung nodules scattered in both lungs. MRI revealed nodules in the liver. Biopsy of the lung revealed invasive carcinoma, possibly moderate to poorly differentiated adenocarcinoma TTF-1 positive ALK negative. The patient's final stage was T2N0M1C stage IVb lung adenocarcinoma.

As far as further diagnostic work-up is concerned, I do recommend a PET scan as well as a brain MRI. I also recommend next generation sequencing efforts to identify patients EGFR, ALK, ROS–1, BRAF, MET, HER-2, RET, NTRK status which can potentially be treated with targeted agents.

If the patient does have EGFR or ALK mutations first-line therapy would be osimertinib for EGFR, alectinib for ALK mutations. If the mutational testing is negative for these two mutations chemo-immunotherapy can be considered. Based on NCCN guidelines and current FDA approvals, chemo-immunotherapy options include **carboplatin plus pemetrexed plus pembrolizumab** OR **carboplatin plus paclitaxel plus bevacizumab plus atezolizumab** OR **carboplatin plus paclitaxel plus pembrolizumab** OR **Nivolumab plus ipilimumab plus paclitaxel plus carboplatin**. If the patient is PD-L1 positive first-line Pembrozulumab alone can be also considered. Among all these combinations I personally prefer carboplatin plus paclitaxel

plus Nivolumab plus ipilimumab combination as outlined in Checkmate–9LA clinical trial. The trial demonstrated clinically significant benefit in overall survival in the chemoimmunotherapy group. This regimen consists of paclitaxel 175 mg/m² plus carboplatin AUC 5 for every 3 weeks 2 cycles and Nivolumab 360 mg every 3 weeks plus ipilimumab 1 mg/kg every 6 weeks until disease progression or unacceptable toxicity or up to 2 years inpatient without disease progression. Again other options are also very reasonable.

Please note, patient's chemotherapy doses may need to be modified based on the patient's liver and kidney functions or patient's general condition and comorbidities. Patients may have chronic hepatitis B infection. This has to be addressed with a gastroenterologist or infectious diseases specialist ASAP since it may lead to reactivation during chemotherapy.

For ROS1, BRAF, MET, HER-2, RET, NRTK mutations there are treatments available especially in the second or third line setting. For ROS–1 crizotinib, for BRAF trametinib plus dabrafenib, for MET exon 14 capmatinib, for RET selpercatinib, for HER-2 trastuzumab, for NTRK gene fusion larotrectinib can be utilized. Please also note that second line chemotherapy options are also available. If first-line chemoimmunotherapy fails and if the patient has no targeted therapy options chemotherapy docetaxel plus ramucirumab can be considered as a second line option.

There are clinical trial options available for this patient throughout the United States. You may search clinicaltrials.gov for this purpose.

I hope you find this information helpful. Again information is provided based on recent data. Please do not hesitate to contact me if you have any questions.

Sincerely,

Mehmet Hepgur, MD
Diplomate American Board of Internal Medicine, Hematology and Oncology

Reference:

NCCN Guidelines. NSCLC Version 8 .2020

Legal Disclaimer:

The Report is an opinion of a medical expert based on the medical information regarding your case that you provide us. The physician rendering the Medical Report will not have the benefit of examining you in person, the ability to order additional tests, or have any information beyond what you provide. The Report is intended to provide you with information to supplement the information you have already received from your treating physicians. The information contained in the Expert Medical Opinion Report shall not be used to substitute for your physician's recommendations. You should discuss the Report with your own doctors, who are responsible for your care.

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