

# TARGETED IMMUNOTHERAPY FOR HEPATOCELLULAR CARCINOMA: A CLINICAL CASE

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## ABSTRACT

**Relevance:** Hepatocellular carcinoma (HCC) is the most common malignant tumor of the liver. HCC is one of the most important problems of the oncology service of Kazakhstan, as it has a progressive course, late detection, low survival, and unfavorable prognosis.

**The study aimed to** evaluate the use of targeted immunotherapy in treating hepatocellular carcinoma in a clinical example.

**Methods:** Clinical case of targeted immunotherapy in combination with Atezolizumab 1200 mg + Bevacizumab 800 mg, once every 3 weeks, in treating HCC in the Regional Oncology Center in Kyzylorda.

**Results:** The first symptoms of liver damage appeared in 2018, at which time HCC was discovered. Viral hepatitis B was diagnosed in 2016. MRI OBP from 15.08.20: a picture of the right lobe of the liver in S5 – 9×7×6 cm, in S3 – 3.7 cm, in S7 – 3.0 cm, in S8 – 2.5 cm. During the follow-up examination (July 2021), the enzyme immunoassay revealed a high angiotensin-converting enzyme (ACE) level of 450.56 IU/ml; the abdominal CT scan showed no deterioration. Later, despite the therapy, ACE increased rapidly: 2,595.3 IU/ml (August 2021) and 2,142.25 IU/ml (September 2021), and the therapy was changed to Regorafenib. ACE continued to rise to 4,405 IU/ml (November 2021) and 18,005 IU/ml (December 2021). A control abdominal CT scan showed a moderate reduction in the size of the tumor.

Taking into account a steady ACE increase, in February 2022, the patient was recommended therapy with Atezolizumab and Bevacizumab. In January 2023, the patient has already received 13 courses, and ACE continued to decrease: 1,932 IU/ml (January 2023), 53.38 IU/ml (February 2023), 16.07 IU/ml (March 2023), and the abdominal CT scan showed positive dynamics.

**Conclusion:** Targeted immunotherapy showed its effectiveness in the described case of inoperable HCC and allowed the patient to continue living, working, and leading an active lifestyle for more than 18 months.

**Keywords:** liver, hepatocellular carcinoma (HCC), targeted immunotherapy, clinical case.

**Introduction:** According to the World Health Organization 2020, more than 905 thousand cases of liver cancer are diagnosed annually in the world. Liver cancer ranks 6<sup>th</sup> among all cancers, accounting for 4.7% of all cancer cases [1]. The National Cancer Registry reported 861 new cases of liver cancer in Kazakhstan in 2020 and 899 cases in 2021. They accounted for 3.5% of all MN cases in 2021 (14<sup>th</sup> place in both sexes) and 4.15% of all MN cases in men (10<sup>th</sup> place) [2, 3]. In 2022, 1003 cases of liver cancer were detected for the first time, which amounted to 4.5 cases per 100 thousand population, with an increase of 7.1% compared to 2021 [4].

Still, the high mortality rate from liver cancer is a problem both globally and in Kazakhstan. In 2020, 830,180 deaths from liver cancer were registered worldwide, which accounted for 8.3% of all deaths from malignant neoplasms (3<sup>rd</sup> place) [1]. In Kazakhstan, 580 deaths from liver cancer were registered in 2020 and 538 cases in 2021, which accounted for 3.9% of all deaths from malignant neoplasms in 2021 (10<sup>th</sup> place among both sexes) and 4.75% of deaths in men (7<sup>th</sup> place) [2, 3]. In 2022, 563 patients died due to liver cancer, which composed 2.9 cases per 100 thousand population, with an increase of 2.6% compared to 2021 [4].

The WHO's forecasts for liver cancer remain disappointing and indicate a rapid increase in the number of new cases – up to 1 million by 2025 worldwide [5].

Hepatocellular carcinoma (HCC) is the most common malignant tumor of the liver. HCC is one of the most important problems of the oncology service of Kazakhstan, as it

has a progressive course, late detection, low survival, and unfavorable prognosis. In 2021, 44 new cases of HCC were detected in Kyzylorda region.

**The study aimed to** evaluate the use of targeted immunotherapy in treating hepatocellular carcinoma in a clinical example.

**Materials and Methods:** The paper presents a clinical case of targeted immunotherapy in combination with Atezolizumab 1200 mg + Bevacizumab 800 mg, once every 3 weeks, in treating HCC in the Regional Oncology Center in Kyzylorda.

**Patient information:** Patient: male, 63 years old, at the time of initiation of treatment, diagnosed with HCC of both lobes of the liver, cirrhosis of the liver in the viral hepatitis B outcome.

**Anamnesis:** The first symptoms of liver damage appeared in 2018, at which time HCC was discovered. Viral hepatitis B was diagnosed in 2016.

**Diagnostics:** MRI OBP from 15.08.20: a picture of the right lobe of the liver in S5 – 9×7×6 cm, in S3 – 3.7 cm, in S7 – 3.0 cm, in S8 – 2.5 cm; chronic cholecystitis with a kink in the cervical area.

**Treatment:** Since 2020, the dispensary registration and start of active treatment. In total, 7 courses of transarterial chemoembolization (TACE) were carried out at Syzganov National Scientific Center of Surgery (Almaty, Kazakhstan), with positive dynamics. On the abdominal CT scan in October 2020, the picture was consistent with HCC,

post-TACE status, cirrhosis of the liver, and adenopathy of porta hepatis. In 2021, the patient began to receive targeted therapy with Sorafenib.

During the follow-up examination (July 2021), the enzyme immunoassay revealed a high angiotensin-converting enzyme (ACE) level of 450.56 IU/ml; the abdominal CT scan showed no deterioration. Later, despite the therapy, ACE increased rapidly: 2,595.3 IU/ml (August 2021) and 2,142.25 IU/ml (September 2021), and the therapy was changed to Regorafenib. ACE continued to rise to 4,405 IU/ml (November 2021) and 18,005 IU/ml (December 2021). A control abdominal CT scan showed a moderate reduction in the size of the tumor.

Taking into account a steady ACE increase, in February 2022, the patient was recommended therapy with Atezolizumab and Bevacizumab.

**Results:** After 7 courses of Atezolizumab 1200 mg + Bevacizumab 800 mg, once every 3 weeks, there was noted ACE decline: 5,163 IU/mL (June 2022), 3,000 IU/mL (No-

vember 2022), as well as a positive trend on the abdominal CT in April 2022.

In January 2023, the patient has already received 13 courses, and ACE continued to decrease: 1,932 IU/ml (January 2023), 53.38 IU/ml (February 2023), 16.07 IU/ml (March 2023), and the abdominal CT scan showed positive dynamics.

Abdominal CT scan (10.01.23): liver cirrhosis; liver formations – the picture is more consistent with HCC, the state after TACE of formations in the projection S, III, V, VIII; without negative dynamics. At this time, the patient continues to receive therapy with Atezolizumab and Bevacizumab. All this time, the patient followed an active lifestyle, continued to work, and was involved in physical fitness. In April 2023, an abdominal CT scan during the follow-up examination showed no negative dynamics; ACE was 5.80 IU/ml. The last ACE result as of July 2023 was 0.72 IU/ml. The patient continues the therapy and tolerates it relatively well.

Table 1 presents the timeline of the described clinical case of HCC treatment.

**Table 1 – Clinical Case Timeline of Immunotargeted Therapy in the hepatocellular carcinoma treatment**

Date	Main events	Measures taken
2016	Viral hepatitis B	self-treatment
2018	HCC	self-treatment
15.08.20	MRI, regular medical check-ups, treatment	7 courses of TACE
2021	Initiation of targeted therapy	Sorafenib
July 2021	IFA on ACE 450,56 IU/ml	Sorafenib
September 2021	IFA on ACE 2142,25 IU/ml	Switching to Regorafenib
February 2021	IFA on ACE 18005 IU/ml	Inception of Atezolizumab and Bevacizumab
November 2022	IFA on ACE 3000 IU/ml	7 courses of Atezolizumab and Bevacizumab
February 2023	IFA on ACE 53,38 IU/ml	13 courses of Atezolizumab and Bevacizumab
April 2023	IFA on ACE 5,80 IU/ml	Continues therapy
July 2023	IFA on ACE 0,72 IU/ml	Continues therapy

**Discussion:** The Atezolizumab + Bevacizumab combination is recommended as a first-line standard of care in patients with advanced HCC [6] and was approved by the European Medicines Agency (EMA) at the end of 2020 [7]. Besides, according to the recommendations of the National Comprehensive Cancer Network (NCCN version 2.2023), the Atezolizumab + Bevacizumab combination is a preferred first-line therapy regimen for HCC [8, 9]. The ESMO guidelines 2021 recommend this combination in first-line HCC therapy with the highest score (5 points). Other therapy regimens are referred to as options [10].

**Conclusion:** Targeted immunotherapy showed its effectiveness in the described case of inoperable HCC and allowed the patient to continue living, working, and leading an active lifestyle for more than 18 months.

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## АНДАТПА

## ГЕПАТОЦЕЛЛЮЛЯРЛЫҚ КАРЦИНОМАҒА АРНАЛҒАН ИММУНДЫҚ МАҚСАТТЫ ЕМДЕУДЕ: КЛИНИКАЛЫҚ ЖАҒДАЙ

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**Өзектілігі:** Бауырдың ең көп таралған қатерлі ісігі – гепатоцеллюлярлық карцинома (ГСС). ГСК Қазақстандағы онкологиялық қызметтің маңызды мәселелерінің бірі болып табылады, өйткені оның прогрессивті ағымы, кеш анықталуы, өмір сүру деңгейі төмен және болжамы нашар.

**Зерттеудің мақсаты** – клиникалық мысалды пайдалана отырып, гепатоцеллюлярлық карциноманы иммундық мақсатты емдеуде қолдануды бағалау.

**Әдістері:** Қызылорда қаласының облыстық онкологиялық диспансерінде Атезолизумаб 1200 мг + Бевацизумаб 800 мг, 3 аптада 1 рет, ХКК емдеуде біріктірілген иммунотаргетациялық терапияның клиникалық жағдайы.

**Нәтижелері:** Бауырдың зақымдануының алғашқы белгілері 2018 жылы пайда болды, сол уақытта ГСС, 2016 жылдан бастап В вирусты гепатиті анықталды. МРТ АҚП 15.08.20: бауырдың оң жақ бөлігінің СҚК суреті S5 – 9×7×6 см, S3 – 3,7 см, S7 – 3,0 см, S8 – 2,5 см. Бақылау кезінде (шілде 2021 ж.) ) КТ АҚК деректері бойынша теріс динамикасыз 450,56 ХБ/мл жоғары АСЕ ELISA индексі анықталды. Кейіннен, терапияға қарамастан, АСЕ деңгейі тез өсуде: 2 595,3 ХБ/мл (тамыз 2021 ж.), 2 142,25 ХБ/мл (2021 ж. қыркүйек). Науқастың терапиясы Регорафенибке өзгертілді. Әрі қарай, АСЕ-нің үздіксіз өсуі байқалады: 4 405 ХБ/мл (2021 ж. қараша), 18 005 ХБ/мл (2021 ж. желтоқсан). Бақылау компьютерлік томографиясы өлімнің қалыпты төмендеуін көрсетеді. АСЕ тұрақты өсуін ескере отырып, 2022 жылдың ақпанында пациентке Атезолизумаб пен Бевацизумабпен емдеу ұсынылды. 2023 жылдың қаңтарында науқас 13 курс алды, АСЕ төмендеуі байқалады: 1932 ХБ/мл (2023 ж. қаңтар), 53,38 ХБ/мл (2023 ж. ақпан), 16,07 ХБ/мл (2023 ж. наурыз), жалғастырумен бірге. АҚК КТ оң динамика.

**Қорытынды:** иммундық мақсатты емдеуде операцияға жарамсыз НСС бар осы науқаста өзінің тиімділігін көрсетті және пациентке 18 айдан астам өмір сүруді, жұмысты және белсенділікті жалғастыруға мүмкіндік берді.

**Түйінді сөздер:** бауыр, гепатоцеллюлярлық карцинома, иммундық мақсатты емдеуде, клиникалық жағдай.

## АННОТАЦИЯ

## ИММУНОТАРГЕТНАЯ ТЕРАПИЯ ПРИ ГЕПАТОЦЕЛЛЮЛЯРНОЙ КАРЦИНОМЕ: КЛИНИЧЕСКИЙ СЛУЧАЙ

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**Актуальность:** Гепатоцеллюлярная карцинома (ГЦК) является наиболее частой злокачественной опухолью печени и одной из важнейших проблем онкологической службы Казахстана, так как имеет прогрессирующее течение и позднюю выявляемость, больные имеют низкую выживаемость и неблагоприятный прогноз.

**Цель исследования** – оценить назначение иммунотаргетной терапии в лечении гепатоцеллюлярной карциномы на клиническом примере.

**Методы исследования:** В статье представлен клинический случай проведения иммунотаргетной терапии в комбинации Атезолизумаб 1200 мг + Бевацизумаб 800 мг, 1 раз в 3 недели, при лечении ГЦК в условиях областного онкологического центра г. Кызылорды.

**Результаты:** Первые симптомы поражения печени появились в 2018 г., тогда же и была диагностирована ГЦК, вирусный гепатит В с 2016 г. МРТ ОБП от 15.08.20 г.: картина ГЦК правой доли печени в S5 – 9×7×6 см, в S3 – 3,7 см, в S7 – 3,0 см, в S8 – 2,5 см. При контрольном обследовании (июль 2021 года) ИФА выявил высокий АПФ – 450,56 МЕ/мл, по данным КТ ОБП – без отрицательной динамики. В дальнейшем, несмотря на проводимую терапию, уровень АПФ стремительно рос: 2 595,30 МЕ/мл (август 2021 г.), 2 142,25 МЕ/мл (сентябрь 2021 года). Пациенту произведена смена терапии на препарат Регорафениб. Далее наблюдался продолжающийся рост АПФ: 4 405 МЕ/мл (ноябрь 2021 г.), 18 005 МЕ/мл (декабрь 2021 г.). На контрольном КТ ОБП – умеренное уменьшение размеров. Учитывая неуклонный рост АПФ, в феврале 2022 г. пациенту была рекомендована терапия препаратами Атезолизумаб и Бевацизумаб. В январе 2023 г. пациент уже получил 13 курсов, отмечается снижение АПФ: 1 932 МЕ/мл (январь 2023 г.), 53,38 МЕ/мл (февраль 2023 года), 16,07 МЕ/мл (март 2023 г.), наряду с продолжающейся положительной динамикой по КТ ОБП.

**Заключение:** Иммунотаргетная терапия показала свою эффективность у данного пациента с неоперабельной ГЦК и позволила пациенту продолжать жить, работать и вести активный образ жизни уже более 18 месяцев.

**Ключевые слова:** печень, гепатоцеллюлярная карцинома (ГЦК), иммунотаргетная терапия, клинический случай.

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