

## ILC 2017: Nivolumab produces durable responses with long-term survival in sorafenib-experienced patients with advanced liver cancer

***New data shows that nivolumab demonstrates a manageable safety profile and promising long-term benefits in sorafenib-experienced patients with advanced HCC***

**April 21, 2017, Amsterdam, The Netherlands:** Results from the CheckMate 040 study presented today found that nivolumab, an immuno-oncology drug which acts by modulating the immune system, produces durable responses with long-term survival rates, regardless of whether or not patients were infected with Hepatitis B or C. Interim results from the study, presented at The International Liver Congress™ 2017 in Amsterdam, The Netherlands, showed that the overall objective response rate (ORR) by blinded independent central review (BICR) was 14.5% and ORR by investigator assessment was 19.3% in sorafenib-experienced patients in the dose expansion phase of CheckMate 040. Responses by BICR were ongoing in 71.4% (15/21) of patients, and the 12-month overall survival rate in this cohort was 59.9%. The safety profile of nivolumab was manageable and consistent with that reported in other tumour types.

Liver cancer, or hepatocellular carcinoma (HCC), is the second most common cause of cancer-related deaths worldwide.<sup>1,2</sup> The prognosis for patients with advanced liver cancer is poor,<sup>2</sup> and the multikinase inhibitor, sorafenib, is the only approved systemic treatment.<sup>3</sup> If the patient is not tolerant or has contraindications for sorafenib therapy, there is currently no standard of care and therefore patients lack effective treatment options.<sup>3</sup> Nivolumab has already increased survival time in different types of cancers, and has become an important treatment option for certain types of kidney, blood, melanoma and non-small cell lung cancer.<sup>4</sup> Preliminary results from the CheckMate 040 study presented earlier this year suggested that nivolumab could be an option for the treatment of liver cancer.<sup>5</sup> Nivolumab is not yet licensed for HCC in the EU.

“The durable responses and survival rates that were achieved with nivolumab are very welcome, especially as the side effects were manageable,” said Prof Bruno Sangro, Head of Liver Unit, Clinica Universidad de Navarra and CIBEREHD, and study author. “These data support the potential of nivolumab in the treatment and stabilisation of advanced liver cancer in those patients who have progressed on sorafenib, with or without chronic viral hepatitis.”

The CheckMate 040 study is a Phase 1/2, multi-cohort, open-label study of nivolumab conducted in patients with advanced liver cancer who were not suitable for surgery.<sup>6</sup> The primary endpoint of the study was ORR by blinded, independent central review. All 145 patients previously treated with sorafenib in the dose-expansion portion of the study were given intravenous nivolumab 3 mg/kg every 2 weeks until the cancer progressed or side effects became intolerable.

Of the 145 patients who had previously received sorafenib, 132 (91.0%) had progression of their cancer and 12 (8.3%) were intolerant of the therapy. The median follow up was 12.9 months in this interim analysis of the dose expansion phase. The median duration of response (DOR) was not yet reached, and 8/21 responders had a DOR of greater than 12 months. The overall median overall survival (OS) was 16.7 months, and it was not reached in those with chronic viral hepatitis B and C. Responses to nivolumab occurred regardless of programmed death-1 (PD-1) ligand expression on tumour cells. Overall, grade 3/4 treatment-related adverse events occurred in 16.6% of patients.

Nivolumab is a programmed-death-1 (PD-1) immune checkpoint inhibitor that is designed to use the body's own immune system to help restore the anti-cancer immune response.<sup>5</sup> It restores T-cell-mediated anti-tumour activity so that the T cells recognise and attack cancer cells.<sup>5</sup>

“The reported median survival of 16.7 months in patients previously treated with sorafenib is promising and it encourages the evaluation of nivolumab in patients affected with hepatocellular carcinoma,” said Prof Alejandro Forner, BCLC group, Liver Unit, Hospital Clinic Barcelona, Spain and member of the EASL Governing Board.

- Ends -

#### **Nivolumab and the programmed-death-1 receptor and ligand**

Nivolumab is a fully human IgG4 monoclonal antibody that binds to the PD-1 receptor.<sup>4</sup> PD-1 receptors on T cells binds to the PD-1 ligand (PD-L1).<sup>7</sup> Cancer cells can sometimes have the PD-L1 on their surface, which helps disguise them from being recognised and destroyed by T cells.<sup>7</sup> Nivolumab can bind to the PD-1 receptor on T cells and block the interaction with PD-L1, thereby blocking the ability of the cancer cell to disguise itself and allowing T cells to be active and attack the cancer cells again.<sup>7</sup> Nivolumab could also cause T cells to attack healthy cells in the body, which can lead to serious or life-threatening side effects.<sup>7</sup>

#### **About The International Liver Congress™**

This annual congress is the biggest event in the EASL calendar, attracting scientific and medical experts from around the world to learn about the latest in liver research. Attending specialists present, share, debate and conclude on the latest science and research in hepatology, working to enhance the treatment and management of liver disease in clinical practice. This year, the congress is expected to attract approximately 10,000 delegates from all corners of the globe. The International Liver Congress™ 2017 will take place from April 19 – 23, at the RAI Amsterdam, Amsterdam, The Netherlands.

#### **About The European Association for the Study of the Liver (EASL) ([www.easl.eu](http://www.easl.eu))**

Since its foundation in 1966, this not-for-profit organisation has grown to over 4,000 members from all over the world, including many of the leading hepatologists in Europe and beyond. EASL is the leading liver association in Europe, having evolved into a major European Association with international influence, with an impressive track record in promoting research in liver disease, supporting wider education and promoting changes in European liver policy.

## Contact

For more information, please contact the ILC Press Office at:

- Email: [ILCpressoffice@ruderfinn.co.uk](mailto:ILCpressoffice@ruderfinn.co.uk)
- Telephone: +44 (0)7841 009 252

## Onsite location reference

**Session title:** General session II and award ceremony I, Hall 5

**Time, date and location of session:** Friday 21 April, 08:30 – 10:30

**Presenter:** Jörg Trojan, Germany

**Abstract:** Nivolumab in sorafenib-experienced patients with advanced hepatocellular carcinoma (HCC) with or without chronic viral hepatitis: CheckMate 040 study (GS010), 09:45 – 10:00

## Author disclosures

Consulting and/or lecture fees from Adaptimmune, Astra Zeneca, Bayer Healthcare, Bristol-Myers-Squibb, Medimmune, Merck, Onxeo, and Transgene.

## References

- 1 World Health Organization. Cancer. Available from: <http://www.who.int/mediacentre/factsheets/fs297/en/>. Last accessed: April 2017.
- 2 World Health Organization. GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. Available from: [http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx). Last accessed: April 2017.
- 3 EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol.* 2012;56:908–943.
- 4 European Medicines Agency. EPAR summary for the public: Opvido (nivolumab). Available from: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Summary\\_for\\_the\\_public/human/003985/WC500189768.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/003985/WC500189768.pdf). Last accessed: April 2017.
- 5 Melero I, et al. Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study. *J Clin Oncol.* 2017;35 (suppl 4S): abstract 226.
- 6 ClinicalTrials.gov. NCT Identifier: NCT01658878. A study to evaluate the effectiveness, safety and tolerability of nivolumab and the combination nivolumab plus ipilimumab in patients with advanced liver cancer (CheckMate 040). Available from: <https://clinicaltrials.gov/show/NCT01658878>. Last accessed: April 2017.
- 7 Bristol-Myers Squibb. How does OPDIVO work inside my body? Available from: <http://www.opdivo.com/advanced-renal-cell-carcinoma/about-opdivo/how-opdivo-works>. Last accessed: April 2017.