

Reports from ESMO 17th World Congress on Gastrointestinal Cancer

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PV-10 shows potential in hepatocellular carcinoma and metastatic liver disease

Two patients – one with hepatocellular carcinoma (HCC) and one with colorectal cancer (CRC) metastatic to the liver – had non-existent liver cancer at more than 40 months follow-up after a single liver injection of PV-10.

Treatment of HCC with chemotherapy, surgical resection, transplantation and other approaches (such as cryoablation, radiofrequency ablation, and chemo ablation) have increased overall survival, but remain suboptimal.

PV-10, a 10% solution of rose bengal originally used as a textile dye and later as an agent to stain necrotic tissue in the cornea, has demonstrated high rates of complete response and durable response in metastatic melanoma. In phase 2 data, presented at ESMO last October, 50% of a subgroup of 28 patients with stage III melanoma who had all their cutaneous lesions injected with PV-10 achieved a complete response and 71% achieved an overall response.

For the current study two cohorts of patients, one with non-resectable HCC (n=6 patients) and the second with other forms of cancer metastatic to the liver (n=7, 3 CRC tumours, 2 non-small cell lung, 2 melanoma and 1 ovarian) underwent a single percutaneous injection of PV-10 (dose 0.25 to 0.50 mL per cm³ lesion volume) guided by CT to one liver target lesion. For the first analysis of five patients, two patients showed no evidence of disease at more than 40 months follow-up according to RECIST and EASL criteria. The first patient was a 68 year old male with



Eric Wachter

HCC (hepatitis B + cirrhosis) alive at 54 months follow-up with no evidence of disease; while the second was a 61 year old male with metastatic CRC alive at 42 months follow-up with no evidence of disease.

Furthermore at up to 54 months follow-up, 10 out of the initial 13 patients were alive. Adverse events were generally limited to injection site reactions and photosensitivity and resolved without sequelae.

"Having liver cancer patients alive at up to 54 months of follow-up with no evidence of disease is remarkable. The study suggests that PV-10 has moved beyond just melanoma and may be agnostic to tumour type," says Eric Wachter (pictured), who co-developed PV-10, adding that the study represents the first report of a chemoablative effect for PV-10 outside melanoma

As with melanoma, the mechanism of PV-10 is believed to be due to local chemoablative effects where the agent enters lysosomes causing tumour necrosis that can stimulate immunological effects. In melanoma, patients injected with PV-10 have shown increased T cells in peripheral blood following injection including CD8+, CD4+, CD3+ and NKT.

Janet Fricker, Medical Journalist.

Reference

Poster Number: P-116. P Goldfarb, MD Russell Low, J Lyon, et al. Phase 1 Study of PV-10 for Chemoablation of Hepatocellular Cancer and Cancer Metastatic to the Liver.

Elderly HCC patients do better on sorafenib

Elderly hepatocellular carcinoma (HCC) patients treated with sorafenib demonstrate longer overall survivals than younger patients, reported the Italian cohort of the observational phase IV Gideon study.

Sorafenib is a multikinase inhibitor used for the treatment of unresectable HCC (uHCC). Two Phase III studies (SHARP and Asia-Pacific) demonstrated significant improvements in overall survival in uHCC patients, the majority of whom had Child-Pugh A with the result sorafenib is now suggested as first-line therapy in HCC patients with advanced-stage disease. The GIDEON study set out to evaluate the safety of sorafenib in uHCC patients under 'real-life' conditions and to gather more comprehensive data on use of sorafenib in patients with Child-Pugh B liver function who had been excluded from clinical trials. Since elderly patients are often underrepresented in clinical trials, the current analysis of the GIDEON study set out to evaluate the tolerability and efficacy of sorafenib in patients older than 70 years.

While the GIDEON study enrolled over 3200 patients to evaluate the safety and efficacy of sorafenib in real life clinical practice, the current analysis explored 278 patients in the Italian cohort, of

whom 141 were older than 70 years and 133 younger than 70 years.

Results showed that the median overall survival was 10 months (8-18) months in the younger age subgroup versus 20 (12-23) months in older patients. Furthermore, elderly patients had a PFS of 6 months versus 4.1 months in younger patients; and elderly patients had a time to progression of 7.6 months versus 5 months for younger patients.

The type and incidence of adverse events (AE) serious and non-serious were similar in the younger and elderly subgroups and in line with the known safety profile of sorafenib. The most serious adverse events were gastrointestinal (diarrhea), dermatologic (hand-foot skin reaction/rash) and fatigue.

Elderly patients had longer overall survival, the authors suggest, due to more advanced disease in the younger subgroup.

Janet Fricker, Medical Journalist.

Reference

P-182 T Zolfino, V Lorusso, S D'Angelo, et al. Hepatocellular carcinoma in elderly patients: Final results of the Italian cohort of GIDEON study.

SIRFLOX: Longer PFS with First-Line SIRT in Patients with Liver-Only Metastases

BARCELONA—"First-line radioembolization in combination with bevacizumab and chemotherapy is able to retard progression in the liver, and it does seem to be safe," said Professor Chris Verslype, MD, a specialist in oncology and hepatology at University Hospital, Leuven, Belgium. Professor Verslype was commenting on results of the phase 3 SIRFLOX trial that evaluated FOLFOX-based chemotherapy and bevacizumab with or without selective internal radiation therapy (SIRT) in metastatic colorectal cancer patients with liver-dominant metastases.

SIRT is a minimally invasive technology approved for inoperable liver cancer in the European Union, the United States, Argentina, Brazil, Australia, and several countries in Asia. It delivers doses of radiation directly to the site of tumours through a hepatic artery catheter infusion of millions of radioactive (yttrium -90) resin microspheres (SIR-Spheres®). While sparing healthy tissue, the microsphere radiation selectively targets liver tumours with a dose of internal radiation up to 40 times higher than conventional radiotherapy.

At this meeting, Professor Guy van Hazel, University of Western Australia, Perth, updated and extended findings recently announced at the ASCO (American Society of Clinical Oncology)



Guy van Hazel

annual meeting, showing the addition of SIRT to have reduced disease progression in the liver by 31%. In the overall population receiving SIRT, the primary endpoint of progression-free survival (PFS) was not significantly longer in the SIRT plus bevacizumab and chemotherapy group ($p=0.43$).

The SIRT benefit in Professor van Hazel's new SIRFLOX data presentation was highly significant. The analysis pertained to 318 patients (159 FOLFOX + bevacizumab; 159 FOLFOX + bevacizumab + SIRT) who had metastases only in the liver. For them, PFS with SIRT added was 8.7 months longer

(FOLFOX + bevacizumab 12.4 months; FOLFOX + bevacizumab + SIRT 21.1 months, hazard ratio 0.64, 95% confidence interval: 0.48-0.86, $p=0.003$). A further analysis of the impact of bevacizumab found that the cumulative incidence of disease progression in the liver was lower for patients receiving SIRT regardless of whether they had or had not received bevacizumab ($p=0.018/p=0.028$, respectively).

"Locoregional therapies like this," noted Professor Verslype, "are gaining interest due to the fact that the liver is the predominant site of disease for most of these [metastatic colorectal cancer] tumours."

Walter Alexander, Medical Journalist.

Meet the Editorial Team



Professor Denys Wheatley is Editor, and is Director of BioMedES. He has strong research ties in Albany, Davis, Auckland, Valencia, Detroit, Budapest, St Petersburg, Heidelberg, Zürich and Hong Kong. He is eager to establish strong interaction with cancer and cell biology teams worldwide, and initiate programmes in the areas in which his expertise lies. His work in cancer research, other scientific fields, with IFCB, and in publishing and scientific communication has led to his receiving awards in recent years.



Dr Richard J Ablin (Associate Editor), is Professor, Pathology, University of Arizona College of Medicine and a Member of the Arizona Cancer Center, Tucson, Arizona. He received the First Award for scientific excellence from The Haakon Ragde Foundation for Advanced Cancer Studies. Dr Ablin discovered prostate-specific antigen (PSA) in 1970. A pioneer of cryosurgery and cryoimmunotherapy, he has extensive experience in cancer research.



Alan Cooper is Assistant Co-Editor – Urology, and is Lead Scientist with the urology research group in Southampton University Hospitals and senior lecturer (albeit with virtually no lecturing burden) in the Department of Biomedical Sciences at Portsmouth University.



Mr Richard Novell is Assistant Co-Editor – Gastrointestinal Section, and is a Consultant Colorectal Surgeon at the Royal Free Hospital. He was a member of the Court of Examiners of the Royal College of Surgeons for eight years and has been an advisor to NICE, NCEPOD and CORESS, the Confidential Reporting System in Surgery.



Dr Miriam Dwek is Assistant Co-Editor – Breast Cancer, she is a Senior Lecturer in Biochemistry at the Department of Molecular and Applied Biosciences, School of Life Sciences, University of Westminster in London.



Prof Mohammed RS Keshtgar BSc, FRCSI, FRCS (Gen), PhD is Assistant Co-Editor – Breast Cancer, and is a Professor of Cancer Surgery and Surgical Oncology, Royal Free London Foundation Trust. His main area of interest is minimally invasive approaches in diagnosis and treatment of breast cancer. His research interest is in sentinel node biopsy, intra-operative radiotherapy, quantum dot nanotechnology in breast cancer.



Professor Geoffrey J Pilkington is Assistant Editor Neuro-Oncology, is a Professor of Cellular and Molecular Neuro-oncology at the Institute of Biomedical and Biomolecular Sciences, Portsmouth. His research focuses on the development of models for the study of intrinsic brain tumours, elucidation of their metabolism and mechanisms underlying diffuse local invasive behaviour.



Farrokh Pakzad is Assistant Editor – Skin Cancer, and is currently Consultant Oncoplastic Breast and Melanoma Surgeon at Royal Surrey County Hospital. His main areas of specialist interest are in the management of breast disease, oncoplastic and reconstructive breast surgery and the management of skin cancers, in particular, melanoma. Farrokh completed his higher surgical training in London, during which he was selected onto the highly competitive National Oncoplastic Fellowship program.



Dr Constantino Carlos Reyes-Aldasoro is Assistant Editor – Image Analysis. He is a Lecturer in Biomedical Image Analysis at the School of Engineering and Mathematical Sciences, City University London. He has developed a unique portfolio of interdisciplinary skills that span from the acquisition of microscopical images to the analysis of biomedical datasets such as magnetic resonance, computed tomography and microscopy to advanced computer programming and website development.



Mriganka De is Assistant Editor – Head & Neck Oncology. Mr De is a Consultant ENT/Head and Neck surgeon at Royal Derby Hospital, Derby. His interest is head and neck cancer with particular focus on management of early laryngeal cancers.



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