Optimal treatment duration defined for trastuzumab

One year of adjuvant trastuzumab should remain the standard of care for HER2-positive early breast cancer patients, concluded both the ‘Herceptin® Adjuvant Trial’ (HERA) and ‘Protocol for Herceptin® as Adjuvant therapy with Reduced Exposure’ (PHARE) trials, presented in the Presidential Symposium Session yesterday.

“The long awaited results constitute a further milestone in the treatment of patients with early breast cancer over-expressing HER2-positive, corresponding to a population of about 12−15% of all cases of breast cancer,” commented Professor Christoph Zeilinski, from the Medical University Vienna, Austria. It was especially appropriate, he added, that the landmark data were presented on October 1 — International Breast Cancer Awareness Day.

Treatment with trastuzumab for 1 year has provided survival benefits to patients with HER2-positive early breast cancer for a number of years and is considered the standard of care. However, the optimal duration of trastuzumab had been much debated due to data from the Finland Herceptin® (Fisher) trial demonstrating improvements in disease-free survival (DFS) with 9 weeks of trastuzumab compared to no trastuzumab. The HER2 positive population in this trial was however, small.

In the PHARE trial, 3,384 patients with HER2 positive early breast cancer who had received at least 4 cycles of (neo-)adjuvant chemotherapy and who were receiving adjuvant trastuzumab for a maximum of 6 months were randomized to either complete 12 months trastuzumab (n=1,690) or to stop trastuzumab at 6 months (n=1,690).

Results showed that DFS was 87.8% in the 12 month group versus 84.9% in the 6 month group (HR 1.28; 95% CI 1.05−1.56).

“The results were inconclusive for the non-inferiority hypothesis. Nevertheless, there was a trend favoring the standard 12 months’ treatment. However there were significant differences in cardiac events favoring 6 months’ treatment,” said the trial presenter, Professor Xavier Pivot from University Hospital of Besançon, France.

Professor Pivot added that a multivariate analysis exploring subgroup would be presented at San Antonio Breast Cancer Symposium (SABCS) in December.

In the HERA trial, 5,102 women with locally determined HER2-positive invasive early breast cancer were randomized after surgery to 1 year trastuzumab (n=1,703); 2 years’ trastuzumab (n=1,701) or to observation (n=1,698). The results showed that the DFS rate in the two arms was comparable (HR=0.99; 95% CI 0.85−1.14; p=0.86).

“The key message for 2012 is that 1 year of treatment with trastuzumab remains the standard of care for HER2 positive early breast cancer patients,” said the HERA trial presenter Professor Richard Gelber, from the Dana Farber Cancer Institute, Boston, USA.

“There was no evidence of long term benefit of 2 years compared to 1 year trastuzumab when administered as sequential treatment following chemotherapy,” said Professor Richard Gelber.

ESMO 2012 breaks all records

ESMO 2012 has proved our biggest and best congress yet with an astonishing 16,394 delegates. Wow! For latecomers with so many attendees there was standing room only in many sessions like the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, all the Young Symposium on genomics in breast cancer, the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, and all the Young Symposium on genomics in breast cancer.

“Wow! For latecomers with so many attendees there was standing room only in many sessions like the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, and all the Young Symposium on genomics in breast cancer.”

“ESMO 2012 has proved our biggest and best congress yet with an astonishing 16,394 delegates. Wow! For latecomers with so many attendees there was standing room only in many sessions like the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, the Presidential Symposia, the ESMO-ASCO Joint Symposium on genomics in breast cancer, and all the Young Symposium on genomics in breast cancer.”
Is there an opportunity for personalized medicine in HCC?

Sorafenib became the standard treatment for advanced HCC five years ago after findings from the SHARP trial showed that treatment with this multitargeted tyrosine kinase inhibitor (TKI) resulted in a 2.8 month improvement in overall survival (OS) compared with placebo. However, since then, results from Phase 3 trials evaluating targeted agents in this setting have been disappointing.

In April 2012, the SUN trial was discontinued after early data showed that sorafenib was inferior to sorafenib + oncolytic vaccinia virus (cervical) (learning from Phase IIb/III trials). This was followed by a similar announcement in December 2011, Bristol-Myers Squibb announced that the WEEF and WEEF/protargol agent, brivanib, did not improve OS as second-line therapy compared with placebo in the BRISK-PS trial. This news was followed by a similar announcement in July 2012, for the BRIL-1 trial of brivanib vs. placebo. Indeed, what also appeared to be a similar trial in July 2012, for the BEAT trial of tivantinib vs. placebo. Although the primary endpoint of time to progression (TTP) showed a small benefit in favor of the overall survival (OS) of the experimental arm, OS was not maintained by the tivantinib arm throughout the study. Furthermore, the overall survival benefit of the experimental arm increased over time, with only 46 and 52 events observed in the placebo arm and the tivantinib arm, respectively, at 12 months.TTP was significant at 4 months. The data for the BRIL-1 trial has been placed in context by world authorities. For example, the ESMO Oncology Pro portal of Clinical Portal for Oncology, ESMO European Society for Medical Oncology.

The decision to stop accrual to this trial was based on the key factor for the risk of decompensation.”

Despite accrual to this trial being stopped early, results showed that the addition of BEV was associated with a significant progression-free survival (PFS) benefit compared with chemotherapy alone (median PFS: 4.7 months vs. 2.4 months; HR: 0.66, 95% CI: 0.48–0.93, P=0.002), and this benefit was maintained across various patient subgroups. The safety profile of bevacizumab + chemotherapy was consistent with previously reported data. However, Dr Masi added that overall survival (OS) data are still immature, with only 46 and 52 events observed in the bevacizumab + chemotherapy and chemotherapy alone arms, respectively.

The decision to stop accrual to this trial based on results from the similarly designed Treatment across Multiple Liver (TAML) trial reported in June 2012, which showed that bevacizumab continued with 2nd chemotherapy was associated with a significant improvement in OS in patients with HCC.

“This is the second randomized trial investigating the impact of bevacizumab continuation beyond first progression,” concluded Dr Masi. “The combination of bevacizumab in combination with standard chemotherapy represents a new treatment option,” he added.

Is there an opportunity for personalized medicine in HCC?

Sorafenib became the standard treatment for advanced HCC five years ago after findings from the SHARP trial showed that treatment with this multitargeted tyrosine kinase inhibitor (TKI) resulted in a 2.8 month improvement in overall survival (OS) compared with placebo. However, since then, results from Phase 3 trials evaluating targeted agents in this setting have been disappointing.

In April 2012, the SUN trial was discontinued after early data showed that sorafenib was inferior to sorafenib + oncolytic vaccinia virus (cervical) (learning from Phase IIb/III trials). This was followed by a similar announcement in December 2011, Bristol-Myers Squibb announced that the WEEF and WEEF/protargol agent, brivanib, did not improve OS as second-line therapy compared with placebo in the BRISK-PS trial. This news was followed by a similar announcement in July 2012, for the BRIL-1 trial of brivanib vs. placebo. Indeed, what also appeared to be a similar trial in July 2012, for the BEAT trial of tivantinib vs. placebo. Although the primary endpoint of time to progression (TTP) showed a small benefit in favor of the overall survival (OS) of the experimental arm, OS was not maintained by the tivantinib arm throughout the study. Furthermore, the overall survival benefit of the experimental arm increased over time, with only 46 and 52 events observed in the placebo arm and the tivantinib arm, respectively, at 12 months.TTP was significant at 4 months. The data for the BRIL-1 trial has been placed in context by world authorities. For example, the ESMO Oncology Pro portal of Clinical Portal for Oncology, ESMO European Society for Medical Oncology.

The decision to stop accrual to this trial was based on the key factor for the risk of decompensation.”

Despite accrual to this trial being stopped early, results showed that the addition of BEV was associated with a significant progression-free survival (PFS) benefit compared with chemotherapy alone (median PFS: 4.7 months vs. 2.4 months; HR: 0.66, 95% CI: 0.48–0.93, P=0.002), and this benefit was maintained across various patient subgroups. The safety profile of bevacizumab + chemotherapy was consistent with previously reported data. However, Dr Masi added that overall survival (OS) data are still immature, with only 46 and 52 events observed in the bevacizumab + chemotherapy and chemotherapy alone arms, respectively.

The decision to stop accrual to this trial based on results from the similarly designed Treatment across Multiple Liver (TAML) trial reported in June 2012, which showed that bevacizumab continued with 2nd chemotherapy was associated with a significant improvement in OS in patients with HCC.

“This is the second randomized trial investigating the impact of bevacizumab continuation beyond first progression,” concluded Dr Masi. “The combination of bevacizumab in combination with standard chemotherapy represents a new treatment option,” he added.

The treatment of head and neck squamous cell carcinoma (HNSCC) continues to challenge oncologists because suitable drug candidates are still limited. Although chemotherapeutic agents are available, curative chemoradiation is the standard of care for early disease, and definitive chemoradiation is the standard of care for advanced disease, most commonly caused by alcohol abuse. Consequently, patients with HCC also have underlying liver disease, most commonly caused by alcohol abuse. In this setting, toxicity and duration of treatment are of utmost importance.

The event will be a 90 min (1 hour and 30 minutes) session of head and neck cancer, Fatima Cardoso early breast cancer, and palliative care, Sandrine Faivre head and neck cancer, Jan Willem Coebergh oncology and palliative care, public health, and Matt Aapro, and palliative care, and Tony O’ Shaughnessy, head and neck cancer, Fudong Zeng early breast cancer, and Tom Hanks, University cancer center, and for oral cancer.

The potential toxicity of drug candidates is significant and will be discussed in depth.

This meeting will focus on the discussion of the potential toxicity of drug candidates, and will also focus on the potential impact of these drugs on the quality of life of patients with HCC.

The event will be a 90 min (1 hour and 30 minutes) session of head and neck cancer, Fatima Cardoso early breast cancer, and palliative care, Sandrine Faivre head and neck cancer, Jan Willem Coebergh oncology and palliative care, public health, and Matt Aapro, and palliative care, and Tony O’ Shaughnessy, head and neck cancer, Fudong Zeng early breast cancer, and Tom Hanks, University cancer center, and for oral cancer.

The potential toxicity of drug candidates is significant and will be discussed in depth.

This meeting will focus on the discussion of the potential toxicity of drug candidates, and will also focus on the potential impact of these drugs on the quality of life of patients with HCC.
Gene therapy in metastatic melanoma: A promising concept?

Results of a pilot-1, proof-of-concept study of AMF, a novel anti-cancer agent that has demonstrated antiangiogenic and anti-proliferative properties in vitro and in vivo models by binding the vascular endothelial growth factor (VEGF), leading to cell cycle arrest, growth inhibition and reduced VEGF expression in activated endothelial and melanoma cells. In this study of 5 patients with disseminated melanoma, AMF was well-tolerated and showed a reduction in tumor volume of 24.1% in the REG arm versus 43.1% and 17% in the placebo arm. The trial was stopped early due to an unexpected adverse event. A phase 2 trial is currently ongoing to further evaluate the efficacy and safety of AMF in melanoma patients.

Molecular imaging in early drug development: Seeing the future

Wednesday’s Special symposium entitled ‘A paradigm shift in early drug development: Imaging biology to move to more patient benefit’ comprised a series of informative and highly educational presentations from experts in the field. Among these was a presentation from Dr Kristoff Muylle, a Nuclear Medicine Physician at Jules Bordet Institute, Brussels, Belgium. Dr Muylle introduced the concept of molecular imaging and its potential to provide a more accurate and personalized approach to cancer treatment. He highlighted the importance of imaging in drug development, emphasizing the need to understand the disease biology and to monitor the response to therapy. He also discussed the role of advanced imaging technologies such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) in the evaluation of new anticancer agents.

Meeting the challenges of clinical trial design in cancer

Despite continuing advances in medicine and drug development, the approval of new cancer drugs to gain regulatory approval is often slower and less secure than previously thought. This is partly due to the challenges faced by clinical trials entering in cancer indications. Specifically, approval of a new drug is often contingent on the demonstration of superior efficacy, compared to the currently approved treatment, in clinical trials that achieve adequately powered endpoints. The delayed approval of effective agents has been reported to delay the development of new cancer drugs, with only 10% of potential candidates moving forward with regulatory approval.

Dr Piccart emphasized the need to adopt innovative strategies to accelerate drug development, making drug development a more efficient and targeted process. This involves utilizing biomarkers to identify patient subgroups who are most likely to benefit from the new treatment and to optimize the design of trials. It also involves using adaptive trial designs, which can adjust the trial based on accumulating data, to achieve faster and more efficient results.

Furthermore, Dr Piccart highlighted the importance of patient engagement and collaboration with patient organizations to ensure that the needs and perspectives of patients are taken into account in the development and approval process. She emphasized the need for continued investment in research and development to drive innovation and to ensure that patients have access to the most effective treatments available.
Gastric cancer – a heterogeneous disease in need of a refined approach

In Sunday’s Presidential Symposium, Professor Peter Lightfoot from the University of Cambridge (UK) and the University Cancer Centre (CCU), Leipzig, presented the findings of a randomized, controlled Phase 3 EXPAND trial of cetuximab in combination with capecitabine as first-line treatment for advanced gastric cancer (ESMO). The rationale for this comes from previous Phase 2 trial data which suggested that cetuximab, an epidermal growth factor receptor inhibitor (EGFR) antibody, in combination with first-line fluoropyrimidine with or without platinum compounds shows promising activity. In the Phase 3 EXPAND trial, patients from 25 countries were randomized to receive 3-week cycles of capcitabine (1000 mg/m² orally days 1–15) and cisplatin (60 mg/m² on day 1 and 250 mg/m² thereafter) (n=455), or the capcitabine/cisplatin combination alone (n=440). Professor Lightfoot explained that baseline characteristics were balanced between treatment arms and that the median duration of capcitabine was 14.9 weeks with a relative dose intensity of 92%, received by 82% of patients. Unfortunately, progression-free survival (PFS) and overall survival (OS) were similar across treatment arms (HR 1.01, 95% CI 0.86–1.19, P=0.78). HR 0.97, 95% CI 0.82–1.14, P=0.67). OS was also comparable across various subgroups.

Professor Lightfoot also explained that the addition of capecitabine showed no benefit compared with cetuximab alone as first-line treatment for advanced gastric cancer, and suggested that further classification of this heterogeneous disease may yield better advances before patient care can make strides.

These data raise the question of whether trials in such a selected patient population should still be conducted. The majority of patients with gastric cancer will present at an advanced stage, and despite advances in diagnostic techniques, strategies and drugs in incidence rates, outcomes remain poor. Without the use of clinical chemotherapeutic agents, survival has not been prolonged, and continues to be investigated, either alone or in various combinations. The results from the EXPAND trial have shown that the efficacy of these agents has reached a plateau. The challenge of this is that every new combination of drugs that target malignant alterations in the gastric cancer cell phenotype. In turn, this will hopefully lead to the development of novel drugs and a better understanding of disease.

The characterization of lung cancer: Choose your targets!

Although lung cancer has long remained the leading cause of cancer-related deaths worldwide, there may be a glimmer of hope for the future treatment of this deadly disease. In his talk, Professor Jean-Charles Soria from the Institut Bergonié Institute in Bordeaux presented compelling data from a Phase II trial evaluating the addition of the anti-EGFR antibody panitumumab (P) to docetaxel and carboplatin (DC) in heavily pretreated patients with advanced non-small-cell lung cancer (NSCLC).

In this trial, patients received docetaxel, carboplatin, or locally advanced esophago-gastric cancer were randomized to EFR targeted therapy or standard-of-care treatment. White blood cell nadirs were lower in the FOLFIRI group, with a higher percentage of patients with grade 3/4 neutropenia. The most common grade 3/4 adverse events were anemia, neutropenia, and thrombocytopenia.

In his talk, Professor Lightfoot explained that although the presence of several genetic alterations has not been shown, for example in squamous cell carcinoma, RET translocation 2% Little evidence on the efficacy of these alterations is available, and until recently, the addition of cetuximab alone to capcitabine and cisplatin was considered to be the standard of care for patients with advanced gastric cancer.

In contrast, patients with HBV may have more readily replicating viruses under immunosuppressive therapy, such as those with HBV with a high rate of viral replication and significant complications; HCV patients under immunosuppressive therapy with antiviral drugs, such as nucleoside analogues, result in significant complications; HCV patients undergoing immunosuppressive therapy, such as those with HBV with a high rate of viral replication, may have more readily replicating viruses under immunosuppressive therapy.

In the latest ESMO Clinical Pharmacology and Toxicology, 2014, 60% with doxorubicin/ifosfamide and 51% with doxorubicin (HR 0.83; 95% CI 0.67–1.03) had a significant difference in overall survival (OS) was identified. Furthermore, the presence of KRAS, a mutation that is involved in tumorigenesis and progression of lung cancer, was associated with a better response to anti-EGFR therapy. This is consistent with previous studies showing that patients with KRAS mutation had a better response to anti-EGFR therapy, indicating that any benefits of an EGFR-targeted therapy are often seen at a higher dose of the drug which could increase response rates as well as toxicity.

The Challenge of Overcoming Resistance in Targeted Therapies for Melanoma

Phase 3 single-agent clinical trials have already shown that monotherapy with BRAF inhibitors is a standard of care for patients with BRAF-mutated advanced melanoma. However, it has now turned to understanding mechanisms of resistance and exploring the scope for combination therapy.

During yesterday’s Special Symposium on Immunotherapy and Anti-angiogenic drugs and their potential role in Patients with BRAF-mutated advanced melanoma with BRAF inhibitors are ongoing. Combinations of BRAF inhibitors with anti-angiogenic drugs or targeting developmental pathways in melanoma are currently being explored. However, the addition of immunotherapy to BRAF inhibitors may help patients to restore efficacy to this drug class, or to achieve durable responses, for instance in BRAF-mutated advanced melanoma.

Despite the promising data collected so far, Professor Soria emphasized the need to move beyond the maintenance of response to drug activity in lung cancer, incorporating clinical architectures, new landscape of molecular drivers, and biomarkers of activity for immunotherapy, in order to further scrutinize patients who are not bothered or are not involved. “Characterization of the genomic landscape of melanoma in the era of anti-angiogenics has been a major achievement,” he said, “but it is not enough to inform newly targeted therapies and treatment planning for patients with BRAF inhibition.”

OUT NOW:

The Latest ESMO Clinical Practice Guidelines

In the next ESMO Clinical Practice Guidelines, recent data on the clinical efficacy and safety of new agents has been incorporated. The guidelines are updated to reflect the latest advances in research and clinical practice, and provide comprehensive, evidence-based guidance for the treatment of various cancer types. The guidelines are designed to help healthcare professionals make informed decisions and improve patient outcomes.

Directions to the ESMO Clinical Practice Guidelines can be found in the “Guidelines” section of the ESMO website.
PARP inhibition: Promise for ovarian and endometrial cancer

Homologous recombination deficiency (HRD) is a defining characteristic of cancers in patients with germline BRCA mutations. This deficiency is exploited by poly ADP ribose polymerase (PARP) inhibitors. Despite their promise, unfortunately, PARP inhibitors provide clear clinical benefit only as monotherapy.

Professor Stan Kaye from the Royal Marsden Comprehensive Cancer Centre, Vienna, Austria, reported the first efficacy results from the phase II study run by the Central European Oncology Cooperative Group (CECOG). The trial compared four targeted, combination-containing regimens. In first-line therapy for HER2-negative metastatic breast cancer, Professor Zuliani, commented, “While seeing a significantly better progression-free survival and overall response rate with paclitaxel + bevacizumab compared to placebo, there is clearly a need for innovative targeted treatments in this patient group.”

OGA has also been observed in endometrial cancer. Professor Kaye stated, although he suggested that the phenomenon is most likely to take a germline disability caused by the characteristic PSEN1 mutation only seen in this disease particularly type 2 in ovarian disease, where their benefit is likely to be greatest.

In vivo studies suggest that PARP inhibitors could also be beneficial for endometrial cancer therapy. Ongoing studies are assessing the use of PARP inhibitors in patients with ovarian and endometrial cancer.

Managing the costs of emerging oncology therapies

ESMO as an organization is not shying away from the current global economic crisis and is conducting comprehensive assessments of the economic impact of health economics in the field of oncology. The Young Oncologists’ breakfast session yesterday was a forum where experts presented the findings of their studies to help the delegates consider the cost of emerging oncology.

Professor Jose Martin-Mirano from the University of Valencia, Spain, told the delegates that the annual EU cost of cancer care was staggering €574 billion. In addition to health care costs, he added, this figure took into account additional factors such as the loss of productivity and mortality. Research showed that European countries are spending between 4% and 5% of health care resources on cancer care.

Across Europe, cancer spending is being萤表扬. Professor Martin-Mirano, The Gazeau-Sauvageon report indicates that the overall burden of cancers assessed in 2008 was €450 billion. Of this amount, €370 billion was spent on cancer-related care, including health care. Co-payments represent a ‘back door’ tax on the sick. Budgets in health and treatment come from differences in income, social status and geography. These are very important characteristics that need to be considered,” said Professor Martin-Mirano.

In the long run, he said, paragranulomatous necrosis, offers the potential for cost savings. “But it comes with implications for large short-term investments,” he explained.

Changes needed to be introduced in the way randomized trials are conducted.

Ms Euna Nicoll, from the London School of Economics (LSE), UK, provided an overview of how Health Technology Assessments (HTA) actually work across Europe. Differences and similarities, she said, exist in the way HTAs assess the same drug.

“The aim of HTA is to provide evidence in healthcare resource allocation and value for money,” said Ms Nicoll. But while HTA may be deemed cost-effective in one country, it may be seen as cost ineffective in another. “We need to identify the reasons for these differences and demonstrate whether they are a consequence of regional specific considerations or HRA processes. We believe that it is likely to be the availability of HRA processes per geography.”

The LSE, she said, has recently undertaken a study on the HTA processes in seven countries: England, Scotland, Sweden, Canada, and Australia.

“Our study showed that some therapies are recommended for different countries and others. For example, in Canada CNS drugs are more likely to be recommended than drugs and cancer drugs, while in Scotland orphan drugs seem more likely to be expected that can reduce cancer and CNS drugs.”

Commenting on the Forum, Professor Jean-Pierre Armand, from the Institut Gustave-Roussy, Villejuif, France, said, “This session really introduced young doctors to the reality of practicing oncology in Europe. They will see quickly that across different countries they don’t have access to the same drugs at the same time for their patients.”

In countries like Lithuania, he said, just €50 per head of the population per year is provided for cancer, whereas in countries like Germany and France prona the €150 per head of the population per year.

One of the reasons for the high cost of drugs, added Professor Armand, has been the failure of drugs to get through phase 3 trials. “We need to be both realistic and make sure that we’re not rushing huge phase 3 trials when we have new indications that drugs may not be effective, and not also running long-lasting trials without knowing what we know of the drugs that work. This was particularly the case with the criticism of oncologists concerned for ALK-positive lung cancer at ESMO 2012,” he said.

Before you go... pick up your copy of the ESMO Pocket Guidelines

First results of TURANDOT Trial

Several PARP inhibitors are now in clinical development and the focus is increasingly turning to their application in germline BRCA associated disease, where their benefit is likely to be greatest. Among those, BM1037 is a new compound and the most potent and selective PARP inhibitor reported to date (up to 700-fold more active on BRCA2-deficient cell lines versus normal cells), with substantial increase in efficacy in vivo in the xenograft. A Phase I trial of BM1037 in the first six patients showed endpoints for progression and preliminary data are promising.

“An adaptive design is a realistic alternative to the data coming from the ongoing trials on modest aspects of the study without undermining the integrity of the trial,” said Professor Grieve.

Aspects of studies that could be modified, he explained, include the number of subjects, study duration, endpoint selection, treatment duration, patient population, number of treatments, number of interim analyses and hypotheses.

An adaptive design requires the trial to be conducted in several stages with access to the accumulated data. “At any stage, the data may be analyzed and next stages redesigned taking into account available data,” explained Professor Grieve.

But the long lay times of months and years that it takes to observe survival endpoints can make it difficult to introduce adaptive design. In Iceland, for example, the most commonly seen response criteria in phase II trials of cancer regimens, could be used instead. “It’s relatively easy to implement adaptive randomization endpoints are available soon after treatment,” explained Professor Grieve.

A good example of adaptive design, he said, was the phase 2 I-SPY-2 randomized breast cancer study in moderates to high-risk primary breast cancer.

“Here a single control arm was compared with multiple drugs, with the idea of identifying biomarker signatures that predict outcomes to drugs. When you see that one agent is doing better than the others you can randomize towards that drug,” said Grieve.

“What’s particularly interesting is the I-SPY-2 is being run by a consortium of 50 academic centers, but the drugs have been provided by 5 different Pharma companies. It showed that very important, in future, to reduce the cost of trials, we should organize more such collaborations,” said Professor Grieve.

At the end of the session audience questions included whether a special GIch system should be introduced for cancer trials. Furthermore, in addition to the cost of the drugs, people felt there was also a need to adjust the cost of the conditions in society, “with the new targeted agents we also need to be able to take into consideration factors such as whether patients can stay in employment. There is a real need to develop novel HRA methodologies, because at present they’re very clunky,” said Professor Grieve.
Bevacizumab is used to treat several types of cancer and most recently has been approved for the treatment of recurrent glioblastomas (GBM) in the United States, United Kingdom and a few other countries. However, for this agent in GBM is not without controversy; the same data that led to its accelerated approval in the United States was rejected by the European Medicines Agency (EMA). Further research to elucidate the true benefits of bevacizumab in GBM is therefore needed and further research to elucidate the true benefits of bevacizumab in GBM is therefore needed.

Yesterday, findings from 2 clinical trials evaluating bevacizumab in GBM were presented as part of several clinical trials are in progress. These include:

1. A multicenter, randomized, double-blind, placebo-controlled study of bevacizumab in GBM patients with unresectable de novo GBM. Despite a trend in improved survival in favor of bevacizumab vs placebo, the trial showed a non-significant difference in overall survival (9% at 24 months; 73% versus 65% at 15 months; 45% versus 50%).

2. A trial of bevacizumab + irinotecan as neoadjuvant treatment for GBM in Europe. The trial showed promising results in terms of improvement in survival; however, due to an imbalance in patient distribution, the trial will not be available until 2015.

In addition, several other clinical trials evaluating bevacizumab in GBM are in progress. These include:

- A trial of bevacizumab + irinotecan in GBM patients with high baseline MMP2.
- A trial of bevacizumab + irinotecan in GBM patients with low baseline MMP2.
- A trial of bevacizumab + irinotecan in GBM patients with intermediate baseline MMP2.

These trials are ongoing and will be presented at future ESMO meetings.

T-DM1 delivers survival benefits in metastatic breast cancer

T-DM1, an antibody-drug conjugate incorporating the microtubule inhibitor DM1, conjugated by a stable linker. T-DM1 is an antibody-drug conjugate incorporating the microtubule inhibitor DM1, conjugated by a stable linker.

The study demonstrated that T-DM1 produced significant benefits in overall survival (OS) and progression-free survival (PFS) compared to irinotecan and cisplatin (IP) in HER2-positive locally advanced metastatic breast cancer patients. Patients with HER2-positive metastases were randomized to receive T-DM1 or IP. The study showed a trend in improved survival in favor of T-DM1 vs placebo, but this was non-significant due to an imbalance in patient distribution. The study will not be available until 2015.

Results showed the median OS was 32.3 months for T-DM1 versus 25.1 months for Cap + Lap (HR=0.60, 95% CI, 0.55−0.77; p<0.0001). PFS by independent review was 6.4 months for T-DM1 versus 4.6 months for Cap + Lap (HR=0.65, 95% CI, 0.55−0.77; p<0.0001).

Adverse events leading to treatment discontinuation were high, with 12% of patients receiving T-DM1 compared to 6% receiving Cap + Lap. Adverse events leading to treatment discontinuation were high, with 12% of patients receiving T-DM1 compared to 6% receiving Cap + Lap.

Results showed the median OS was 32.3 months for T-DM1 versus 25.1 months for Cap + Lap (HR=0.60, 95% CI, 0.55−0.77; p<0.0001). PFS by independent review was 6.4 months for T-DM1 versus 4.6 months for Cap + Lap (HR=0.65, 95% CI, 0.55−0.77; p<0.0001).

Excellent response rates were observed in patients receiving T-DM1, with 23% of patients achieving a complete or partial response. Excellent response rates were observed in patients receiving T-DM1, with 23% of patients achieving a complete or partial response.

Both treatment arms, added Professor Verma, were well-balanced.

The biomarker hENT1 has already been confirmed suitable for gemcitabine therapy.

The study showed that evaluating bevacizumab activity in GBM was successful, with high baseline MMP2 was associated with an 83.3% chance of response. The study showed that evaluating bevacizumab activity in GBM was successful, with high baseline MMP2 was associated with an 83.3% chance of response.

Emeline Tabouret from AP-HM, Timone Hospital, Marseille, France, presented data from her institute on the use of bevacizumab in GBM. The study showed that evaluating bevacizumab activity in GBM was successful, with high baseline MMP2 was associated with an 83.3% chance of response.

Given the growing importance of genetic profiling, future research to elucidate the true benefits of bevacizumab in GBM is therefore needed. Further research to elucidate the true benefits of bevacizumab in GBM is therefore needed.