SMR Society for Medicines Research

NEWSLETTER

Issue 1/2006

WELCOME

Welcome to this new-look newsletter, which reflects our continuing efforts to improve the service the SMR provides to its members. As part of this process, we have now introduced membership cards, your card should be enclosed. Please bring it along to all future meetings you attend. The next meeting will be a new venture for us – as part of the celebration of our 40th Anniversary, our December meeting will be part of the UK's largest Biotech conference – Genesis. The symposium will include the SMR Award, which this year goes to a medicine in the news at the moment – Avastin. We will also be holding our annual general meeting – see enclosed agenda.

Alan Palmer
Chairman

SOCIETY CELEBRATES 40TH ANNIVERSARY

The SMR celebrates its 40th Anniversary this year. Originally called the "Society for Drug Research", the inaugural meeting was held on 28th September, 1966 at the Royal Pharmacological Society of Great Britain. The Society gained Charitable Status in 1977 and changed its name to the "Society for Medicines Research" in 1994.

To mark 40 years of the SMR, we have organised a special meeting in conjunction with the London Biotechnology Network and UK Trade and Investment. The event will be held at the DTI conference centre in Victoria Street on December 11. The programme begins with an overview lecture about future strategies for medicines research and its funding in Europe, followed by the 2006 SMR Award lecture. This year the award will be presented to Dr Napoleone Ferrara of Genetech for the development of the anti-VEGF antibody Avastin (bevacizumab) for the treatment of metastatic colorectal cancer and other types of cancer. The remainder of the meeting has been designed to showcase the best of medicines research in the UK and highlights a number of drug discovery success stories from several UK biotech companies.

Entry to the event entitles SMR members attend a wine reception at the London Stock Exchange in the evening and discounted entry to Genesis, the UK's largest biotechnology conference, on December 12th.

The 2006 SMR award prize-winner: the anti-VEGF antibody Avastin (bevacizumab)

The growth of tumours is often associated with a large increase in blood supply which nourishes the tumour and thus sustains progression . This observation suggested the existence of factors that stimulate blood vessel proliferation and raised the possibility of using such factors as targets for the discovery of new medicines to treat cancer. Although the identification of such factors has proven to be difficult, it is now known that one of the key regulators of both of normal and abnormal blood vessel growth is vascular endothelial growth factor (VEGF). In 1993, it was shown that a monoclonal antibody that targeted VEGF suppresses tumour growth in experimental *in vivo* models. This then led to the development of bevacizumab (Avastin; Genentech), a humanized variant of the anti-VEGF antibody, as an anticancer agent. Avastin has now been approved in Europe and the USA as a first-line therapy for metastatic colorectal cancer. Clinical trials are currently underway to establish its utility in a range of other types of cancer. Avastin clearly represents an exciting new approach for the effective treatment human malignancies. Dr Ferrara will provide a description of how Avastin made it to market at our December meeting.

Dates for your diary:
SMR Meetings in 2007

1. Filling the innovation gap in drug discovery. 8th March 2007. NHLI, London.
2. Neurodegeneration. 14th June 2007. Eli Lilly, Windlesham, Surrey.
3. Emerging therapies for respiratory disorders, 11th September 2007. Hinxton Hall, Cambridge.
4. Recent disclosures of clinical drug candidates. 6th December 2007. NHLI, London.

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REPORTS OF PREVIOUS MEETINGS:

Therapeutic Approaches towards the Treatment of Gastrointestinal Disorders

An international panel of speakers together with around 60 delegates was brought together by the The Society for Medicines Research's symposium on *Therapeutic Approaches Towards the Treatment of Gastroinstestinal Disorders*, held on September 21, 2006 at the National Heart and Lung Institute. The focus of the conference was to discuss therapeutic strategies taken towards the treatment of inflammatory bowel disease, acid related disorders and irritable bowel disease. Dr Pfannkuche (Novartis) delivered the opening lecture which detailed the research and development of Tegaserod, a 5-HT_4 receptor agonist which is currently being used in the clinic as a gastroprokinetic for the treatment of IBS with constipation (cIBS) and chronic idiopathic constipation. Dr O'Mahony from University College, Cork delivered the second lecture which focussed on the growing scientific interest around the role of bacteria in the treatment of gastrointestinal disease. Although the clinical data supporting the impact of probiotic consumption on disease symptoms are conflicting and are often confounded by small numbers, Dr O'Mahony presented data demonstrating the imbalance in cytokine signallying networks is normalised following the consumption of a single commensal bacterium, *Bifidobacterium infantis* 35624. Dr Sanger (GSK) opened the afternoon session with a review of the role of neuropeptides in the control of gastrointestinal motility. Dr Sanger reviewed not only the clinical studies reported with Motilin but also the emerging data supporting the role of Ghrelin and the recently reported peptide obestatin on GI motility. Dr Brown (UCB) reviewed the use of tumor necrosis factor α inhibitors (TNFα) in the treatment of chronic inflammatory diseases, including Crohn's disease. The mechanisms of actions four anti-TNFα agents were compared in several in vitro systems. Interestingly, whilst all four agents neutralised soluble TNFα and bound to and neutralised membrane TNFα, differences were observed in their respective ability to mediate complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC). Dr Andersson gave a highly entertaining lecture focussing on the trials and tribulations of developing effective inhibitors of gastric acid secretion. The scientific rationale for improved clinical efficacy observed with the single enantiomer of the proton pump inhibitor (PPI) omeprazole, S-omeprazole (Nexium), was discussed together with the more recent work in the field of potassium-competitive acid blockers (P-CAB's). In contrast to PPIs it was postulated that the P-CAB's would demonstrate a faster onset of action due to their ability to reach high plasma concentrations. Clinical data was presented on AZD0865 which has demonstrated excellent efficacy with respect to its ability to lower intragastric pH. Unfortunately the clinical data generated to date has so far failed to differentiate Nexium and AZD0865 with respect time of healing or symptom relief. The final lecture of the day was delivered by Robert Egan of Milennium. The lecture focused on the role of alpha4beta7 integrin in the development of Crohn's disease and ulcerative colitis. Alpha4beta7 is the dominant integrin that directs memory T cells to the gut and whilst the dual alpha4 antibody Tysabri has demonstrated clinical efficacy it is postulated a selective antibody would be devoid of the clinical liability of developing progressive multifocal leukoencephalopathy (PML). Clinical data was presented on the first alpha4beta7 selective antibody, MLM0002, which demonstrated efficacy against the primary endpoint of induction of remission measured by ulcerative colitis clinical score, modified Baron score and rectal bleeding.

Translational Sciences – Turning Drug-like Molecules into Medicines

On June 15, 2006, the Society for Medicines Research held a one-day meeting in Harlow, United Kingdom, entitled Translational Sciences – Turning Drug-like Molecules into Medicines. The meeting brought together speakers from Europe representing the pharmaceutical industry and provided an overview on some of the latest approaches in a range of areas such as predictive toxicology, translational biology, in vitro-in vivo extrapolation, PK/PD modelling, and the use of biomarkers and surrogate endpoints.

Recent Disclosures of Clinical Drug Candidates

On December 8, 2005, the Society for Medicines Research held a one-day meeting in London, United Kingdom, entitled *Recent Disclosures of Clinical Drug Candidates*. The meeting brought together speakers from Europe representing the pharmaceutical industry and provided an overview of some the latest approaches being taken in a range of therapeutic areas such as oncology, inflammation, CNS disease and reproductive medicine. The meeting proved to be very popular. Several pharmaceutical companies provided a fascinating illustration of the strength of research and the diversity of research strategies used to discover and develop new medicines.

Cancer Treatments for the New Millennium

The SMR Symposium *Cancer Treatments for the New Millennium* was held on March 9, 2006, at the National Heart and Lung Institute, Imperial College London. The program presented an international line-up of speakers representing academia, biotech and large pharma to discuss the development status of a number of new innovative treatments for the treatment or prevention of cancer. Presentations also focused on how new technologies are being applied to the design of the next generation of cancer drugs and the fundamental biological challenges that must be addressed in attempting to discover effective new treatments.

A full report of these meetings have been published in Drug News & Perspectives. The full article, together with a webcast of the meetings, are available on the SMR website.