Among objective responders, the median response duration was nine months for the overall group and 11 months for double-resistant patients. An objective response occurred in 8% of patients overall and in 9.5% of the double-resistant patients. An additional minor response occurred in 8% overall and in 6% of the double-resistant group. Progression occurred in 43% of the overall group and in 56% of double-resistant patients. The median overall survival was 10.3 months overall and 10.1 months for the double-resistant group.

Interesting results...

'Trabectedin has been a reasonably widely studied drug in sarcomas, particularly in patients with advanced disease,' said Robert S. Benjamin, who chairs the Sarcoma Medical Oncology Department at the University of Texas M.D. Anderson Cancer Center (http://www.mdanderson.org) in Houston, Texas, and is on the Sarcoma Panel for the National Comprehensive Cancer Network (http://www.nccn.org). 'Although the response rate is relatively low, patients seem to have fairly long periods of time to progression, so that there's some control of the rate of progression,' he said. 'This is probably an effective strategy for trying to treat these tumours.'

Jerome W. Yates, the National Vice President for Research at the American Cancer Society (http://www.cancer.org) agrees up to a point. 'The findings are interesting but not exciting,' he said. 'The biggest problem with studies done in sarcomas is that there are a variety of different diseases. To draw conclusions regarding the [feasibility of trabectedin] in soft-tissue sarcomas in the future is pretty difficult when you look at the relatively small numbers.'

Neurogenomics of mice and men

Nina Keegan, BMN News

A longstanding interest in isolated populations and population genetics has led Nelson Freimer of the University of California, Los Angeles (http://www.ucla.edu) to propose the establishment of the 'Human Phenome Project'.

Phenotype information

As the sequencing of the human genome presents the opportunity for research to identify and assign function to each identified gene, it is hoped that a similar phenome project will enable gathering of detailed information on phenotypes, to further understand genes and their behaviour. Current methods for defining phenotypes can be inadequate, and it is only by developing a more comprehensive phenotyping process that full advantage can be taken of genotyping studies.

For example, current research into the genetic contribution to disease might be held back by the inability to identify phenotypes in the genomes under investigation. It is hoped that a database of phenotypic data will help to overcome this.

One possible component of the phenome project is the integrated genetic and neurobiologic investigation of the vervet monkey (*Cercopithecus aethiops*), notes Freimer, who spoke on the topic at the *5th Brain Research Symposium* in New Orleans, USA (6–7 November 2003). Several decades of study in vervet colonies has demonstrated heritability for a range of behavioural phenotypes. The vervet colony study is equivalent to human population isolates and thus particularly powerful for genome-wide mapping of such phenotypes. Furthermore, the results should be more meaningful than those taken from a more distantly related animal to the human, such as the mouse.

Brain structures

However, these phenomic efforts in non-human primate models are still in the primary stages, and much effort is still needed to complete the full sequencing. Current research focuses specifically on those phenotypes relating to mood, temperament and anxiety. Along with his collaborators, Freimer is developing the tools to undertake full genomic analysis of the primates and to attempt to tie the findings in with much broader information on the specific phenotypes. For example, by undertaking brain

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tissue analysis for gene expression, neuroimaging, pharmacologic intervention and behavioural assessments (such as intruder challenge and novelty response tests), analyzing the data together and interpreting the results as a whole, it will enable a more complete understanding of the processes of brain behaviour.

For Freimer's own research interests, the study specifically provides the necessary information that enables him to better understand brain structures – their size and shape. It is well known that these structures are highly heritable, but it remains to be seen which genes are responsible. It is hoped that collating the data from the colony will make it possible to identify the loci responsible for the variability. From identifying the genes that have a role in a whole range of behavioural traits, the ultimate aim is to ascertain whether these are comparable to genes in humans and whether they function in a similar manner in human brain processes.

Robin Ganellin gives his views on medicinal chemistry and drug discovery

Interview by Stephen L. Carney

C. Robin Ganellin, FRS, Smith Kline & French Professor of Medicinal Chemistry, University College London

Robin Ganellin was born in East London and studied chemistry at Queen Mary College, London, receiving a PhD in 1958 under Professor Michael Dewar for his research on tropylium chemistry. He joined Smith Kline & French Laboratories (SK&F) in the UK in 1958 and was one of the co-inventors of the revolutionary drug cimetidine (Tagamet®) He subsequently became Vice-President for Research at the company's Welwyn facility. In 1986 he was awarded a DSc from London University for his work on the medicinal chemistry of drugs acting at histamine receptors and was also made a Fellow of the Royal Society and appointed to the SK&F Chair of Medicinal Chemistry at University College London, where he is now Emeritus Professor of Medicinal Chemistry. Professor Ganellin has been honoured extensively, including such awards as the Royal Society of Chemistry Award for Medicinal Chemistry, their Tilden Medal and Lectureship and their Adrien Albert Medal and Lectureship, Le Prix Charles Mentzer de France, the ACS Division of Medicinal Chemistry Award, the Society of Chemical Industry Messel Medal and the Society for Drug Research Award for Drug Discovery. He is a past Chairman of the Society for Drug Research, was President of the Medicinal Chemistry Section of IUPAC, and is currently Chairman of the IUPAC Subcommittee on Medicinal Chemistry and Drug Development.

What factors influenced you to begin a career in chemistry?

I suppose it goes back to one's education system and how one reacts to it. At school I found my abilities were skewed very much towards the sciences. I came pretty close to the top in biology and maths and down at the bottom of the class in history and languages. My father and one of my mother's brothers were chemists so you could say there was a genetic determinant. Actually I was very keen on biology and natural history was a sort of hobby for me. I suppose if I was totally free I would have gone on to be a biologist but at the time I felt I didn't know how I would earn my living as a biologist – I didn't know any biologists, but I knew chemists so I went into chemistry.

What aspects of your career have given you most pride professionally and personally?

I find that making discoveries is very exciting; it is the most stimulating part, and especially succeeding where you think others may have failed and doing something really new. I saw this during my PhD studies, when I discovered, partly through chance and partly through reading, that just by treating cyclooctatetraene (an eight-membered hydrocarbon ring) with potassium permanganate solution I could isolate the tropylium cation (which is a seven-membered ring). So you go from C8 to C7 in what apparently was one step. Then I worked out the mechanism and found that incredibly exciting, especially knowing that during the second World War, a famous German chemist called Walter Reppe had been making cyclooctatetraene and then studying its reactions. He had suggested most improbable mechanisms and this little thing we had discovered led to a clear understanding of what those mechanisms must have been. I find it remarkable that our education system can take, in my case, a schoolboy and in a few years produce someone capable of making what I thought were important discoveries.

You asked me, in terms of my career, what has given me most professional pride; that has to be Tagamet®, which was a fantastic achievement. I think that I was very fortunate that things worked out, and it was very difficult to accomplish. I remember after it had come on to the market, going to a family occasion and one of my uncles coming up and saying, thank you. I said 'thank me for what?' and he replied 'for what you have done for me. I've been in bed for two weeks in terrible pain with an ulcer and I've taken this medicine and here

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