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Editorial Comment

The future of clinical cancer research: who's teaching the next generation? The Flims–Vail model

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For the past 5 years, the Federation of European Cancer Society (FECS), the American Association of Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO) have brought together a group of young and motivated oncology trainees to Flims, Switzerland to participate in the 'Workshop on Methods in Clinical Cancer Research'. This week-long, intensive course provides guidance in the principles and practice of oncology clinical trial design and implementation.

The origins of the Workshop lay in the vision and foresight of two men, Dr. Daniel D. Von Hoff and Dr. Charles A. Coltman, Jr. In 1994, they opened discussions between the AACR and ASCO to address the critical shortage of young, translational clinical investigators who conceive and conduct clinical trials of new anticancer agents. They recognised that insufficiencies in the design and direction of clinical cancer trials were responsible for the abandonment of many promising avenues of research and in delaying the introduction of effective new therapies to patients. Their work ultimately resulted in the AACR and ASCO establishing the workshop 'Methods in Clinical Cancer Research' to tutor young clinical investigators in effective, clinical trial design. In 1996, the first Workshop was held in Park City, Utah; subsequent Workshops have convened annually in Vail, Colorado. Funding for these courses originated from a meeting grant from the National Cancer Institute (NCI) along with funds raised by AACR and ASCO from the pharmaceutical industry and other sources. The problems facing clinical research in the United States of America (USA) and their potential solution were subsequently highlighted in a series of articles in the *Journal of the American Medical Association* which revealed a 35% decline in the number of physician scientists between 1984 and 1999 [1–3].

In 1997, Dr Jean Pierre Armand participated as a faculty member and mentor in the Vail workshop, and recognised the need for a similar course in Europe. He approached the FECS and advocated collaboration with the AACR and ASCO to organise and institute a second annual Workshop in Europe. The first European Workshop was held in Flims, Switzerland in 1999 funded by an educational grant from the NCI together with funds raised from the pharmaceutical industry and European cancer societies.

What makes the 'Methods in Clinical Cancer Research' Workshop distinctive? The answer lies in the faculty, the unique format of the course with its various teaching methods, and the expected implementation of novel research protocols. Faculty members are internationally recognised clinicians, translational researchers and biostatisticians with extensive experience in the design and institution of clinical trials. The faculty members give up 1–2 weeks of their time each year to teach and mentor participants. The course format consists of three main parts. Firstly, lectures encompassing all aspects of phase I, II and III clinical trial design, with topics ranging from pharmacokinetics and biostatistics to the Helsinki declaration and issues surrounding informed patient consent. These lectures afford students a sound theoretical grasp of the design and conduct of clinical trials. Secondly, smaller interactive discussion

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groups that allow for a more intense discussion with experienced clinical investigators on a variety of special topics such as pharmacogenomics, correlative studies including laboratory and imaging correlates, trial designs of cytostatic agents, and novel biological endpoints. Thirdly, the defining element of the Vail–Flims workshops, as well as the core activity, is the development of a clinical research protocol. This involves participants developing their own clinical studies from a concept sheet to a completed trial protocol by the week's end ready for submission to a local ethics committee. The concept and feasibility of the proposed protocol forms a key part of the student application and selection process. Given this, the support and commitment of a mentor at the student's home institution is essential, and written assurance from the mentor must be provided that the participant will be given the opportunity to instigate and lead the trial that is developed at the workshop. Organisers generally favour proposals for phase I and phase II trials, due to the feasibility of being led by the participant and being implemented at a single (or a few) institution(s); phase III trials which are generally large, multicentred trials, may require many years to implement and be difficult for the participants to take a leading role in managing given their nature.

The primary educational vehicle is the protocol development groups, consisting of 7–10 students which are mentored by 2–3 clinical investigators and a biostatistician. The groups meet daily throughout the workshop allowing for rigorous interaction and discussion between students and faculty members regarding each protocol's design. Critical evaluation of each proposed trial continues throughout the week's development sessions. The initial sessions identify any major problems ranging from scientific to clinical to logistic, thus allowing for modifications to the trial design to occur as early as possible. A finalised, approved protocol concept sheet serves as the template for writing the final protocol. Faculty members are always available and extensive one-to-one mentoring is thus provided outside these sessions to help individuals develop their protocols. Given the task of writing a full clinical protocol and the time involved, the week is a period of intense activity and work for both students and faculty, with students actively putting into practice what they are learning.

The workshops do not end at the conclusion of the week; faculty members continue to correspond and provide mentoring and support for students to ensure that their trials are implemented. In addition, a Flims alumni club has been established with its own website (http://www.flimsalumni.org) to help keep individuals in contact and to promote the active involvement of young oncologists in clinical cancer research [4]. Given the international nature of the workshops, participation fosters a spirit of international camaraderie and cooperation, allowing students and faculty to interact and learn from the experiences of others. It is also anticipated that the workshops will lead to future collaborations between students as they develop and progress in their careers. The success of the Vail–Flims workshops has led the organisers to establish a similar workshop for those living in South East Asia and Oceania; it is hoped that the first workshop will occur in Cairns, Australia in the near future. In addition, this innovative and unique workshop could serve as a model that could be followed by other clinical specialties.

To date, over 1000 students, from all six continents, have participated in the Vail–Flims workshops. According to the FECS survey, the follow-up data from the three classes (1999–2001) of the Flims workshop are extremely encouraging (Prof. Nu Viet Vu, University of Geneva Faculty of Medicine, Switzerland, pers. commun). Of the fellows who had returned the survey questionnaire (71–76%), it was found that approximately 50% of the protocols developed during the workshop were submitted within 2 years to the local Ethics Review Committees (ERCs). Of these protocols, 94% were approved by the local ERCs and 76% were implemented at the participants' local institution. In addition, most workshop participants have also been very productive; they were actively involved in other clinical protocols aside from the one they have developed at the workshop. Within 1 year of the workshop, approximately 40% of the participants had one protocol and 30% two or more protocols submitted and implemented at their local institution. By 2 and 3 years after completion of the workshop, the number of participants who had two or more protocols submitted and implemented have risen to 48 and 74%, respectively. In addition, attesting to the quality of these protocols is the fact that, not only were they implemented, but also most of these protocols were able to generate their own financial support. Despite the clear success of the workshop, approximately half of the protocols developed at these workshops are never submitted to the local ERCs. Many difficulties have been encountered in the protocol submission process for various reasons, including the lack of access to the necessary agent, scientific disagreements between clinical investigators at the local institutions and lack of funding for the study and problems with the pharmaceutical companies that are involved. Not unexpectedly, due to the immaturity of many of the studies, relatively few studies have been presented at national or international meetings (2–18%) or published in peer-reviewed journals (approximately 5%). However, there have been some impressive accomplishments; a phase I trial developed at the 1999 Flims workshop has recently been published [5] and a graduate of the Flims 2001 workshop received the Pain management merit award at the 2003 ASCO meeting [6].

In conclusion, the fundamental aim and guiding principles of Drs Von Hoff and Coltman in establishing the workshop were to encourage, train and develop the next generation of oncologists in clinical research. There are encouraging signs that their vision of high quality clinical and translational trials, led by workshop alumni to improve the therapeutic options for patients, is happening. However, although the seeds are sowed at Vail and Flims, their nurturing afterwards is critical, and support and mentoring must be provided, both locally and nationally, by universities, governments and the pharmaceutical industry. Only if this happens will the full potential of the Vail–Flims model be realised.

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