

The Italian Network for Tumor Biotherapy. Sharing visions, goals and efforts at European level

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ABSTRACT

In the context of the Scientific Week 2008 of the Organization of the European Cancer Institutes, the Italian Network for Tumor Biotherapy (NIBIT), within its initiatives sponsored by *Alleanza Contro il Cancro*, the Italian Network of Comprehensive Cancer Centers has contributed to organize the Workshop of the European Networks for bio-immunotherapy of tumors. Representatives from the Nordic Center of Excellence for the Development of Anti-Tumor Vaccines (Sweden), the German Network of Immunotherapy of Tumors (Germany), the Biotherapy Development Association and NIBIT gathered to present their organization and ongoing scientific activities, as well as to identify common strategies and shared efforts to push the field of cancer bio-immunotherapy forward at a European level. This article briefly summarizes the history and objectives of NIBIT, along with the actions so far taken by the Network.

Introduction

Increasing knowledge on the molecular mechanisms involved in neoplastic transformation, the biology of cancer cells, and the immunological mechanisms regulating tumor-host interaction allows us to identify and to apply in the clinical setting novel and eventually more effective bio-immunotherapeutic strategies in cancer patients¹. However, for their optimal clinical development, and for their swift translation from the laboratory to the clinical setting, these new therapeutic approaches require a strict cultural and operative interaction among different professionals involved in the clinical, regulatory and industrial fields. Thus, a shared effort is mandatory to evaluate with due appropriateness, rapidity and scientific rigor the biological and clinical efficacy of novel treatments that become available^{2,3}. Nevertheless, while cancer bio-immunotherapy is consolidating its role as an additional and powerful option in the comprehensive treatment of cancer patients, it raises new and specific procedural, ethical, and legal challenges to its broader clinical application⁴. Therefore, the efficient clinical development and application of new modalities of cancer bio-immunotherapy is often difficult for large research entities and in most cases impossible for small research units.

On these premises, and to answer a need strongly felt by the Italian academic, industrial and regulatory community, the NIBIT (acronym for the Network Italiano per la Bioterapia dei Tumori - Italian Network for Tumor Biotherapy) was created in 2004⁵. The NIBIT has been given legal status as a non-profit association on September 2006.

Key words: *biotherapy, cancer, immunotherapy, networks.*

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Results

The initial discussion among the founders of the NIBIT focused on the identification of its main statutory goals and objectives that were identified in the following: a) to promote and foster a stronger scientific and operative interaction among professionals belonging to academia, the biotech/pharmaceutical industry, and regulatory bodies; b) to develop innovative, multicenter clinical studies of cancer bio-immunotherapy at the national level; c) to set up initiatives to inform patients about potentials and limitations of cancer bio-immunotherapy and about ongoing clinical trials.

At present, the NIBIT is coordinated by a Board of Directors in office from 2006 to 2009 that includes Dr. Giorgio Parmiani (Milan) as President, Dr. Michele Maio (Siena) as Secretary/Treasurer, and Drs. Paolo Antonio Ascierto (Naples), Filippo Belardelli (Rome), Roberto Camerini (Pomezia), Mario Paolo Colombo (Milan), Paola Queirolo (Genoa), Ruggero Ridolfi (Forlì), Vincenzo Russo (Milan) as Councillors.

As of today, the NIBIT has more than 60 official members that represent over 40 academic, regulatory and industrial groups/bodies including: *Academic*, Azienda Ospedaliera Universitaria Senese (Siena); Azienda USL di Forlì, Azienda Ospedaliera Ospedale Niguarda Cà Granda (Milan); Centro di Riferimento Oncologico, IRCCS (Aviano); Fondazione San Raffaele del Monte Tabor (Milan); INRCA, Istituto di Ricovero e Cura a Carattere Scientifico (Ancona); Istituto Europeo di Oncologia, IRCCS (Milan); Istituti Fisioterapici Ospedalieri "Regina Elena", IRCCS (Rome); Istituto "Giannina Gaslini", Ospedale Pediatrico IRCCS (Genoa); Fondazione IRCCS Istituto Nazionale dei Tumori (Milan); Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione "G. Pascale", IRCCS (Naples); Istituto di Ricerca e Cura del Cancro, IRCC (Candiolo); Istituto Scientifico Tumori, IRCCS (Genoa); Istituto Tumori "Giovanni Paolo II" IRCCS, Ospedale Oncologico (Bari); Policlinico "San Matteo", IRCCS (Pavia); Temple University (Philadelphia, USA); Università degli Studi di Bologna; Università degli Studi di Messina; Università degli Studi di Padova; Università degli Studi di Perugia; Università degli Studi di Torino; *Regulatory*, Agenzia Italiana per il Farmaco, AIFA (Rome); Istituto Superiore di Sanità, ISS (Rome); *Industry*, Merck, Sigma-tau.

Noteworthy, though the NIBIT has been just recently founded and initiated its activities, the geographic distribution of its affiliated groups has an extensive distribution nationwide (Figure 1). This active participation into the NIBIT project has been fostered also by national yearly scientific meetings of the Network⁵ that have been held at the Certosa di Pontignano, a Tuscan monastery built by the Chartusian Order in 1343 and located on the border between the town-states of Florence and Siena, which has been identified as the permanent venue for this initiative (Figure 2). The aim of



Figure 1 - Distribution of NIBIT members at national level.



Figure 2 - The main cloister of the Certosa di Pontignano (Siena, Italy).

the annual meeting of the NIBIT is to discuss scientific pre-clinical and clinical advancements in different fields of cancer bioimmunotherapy. In the course of the four national congresses that took place so far, several major topics were covered and discussed including: a) new antigens and cytokines; b) therapeutic antibodies and recombinant constructs; c) molecular and cellular mechanisms of tumor escape; d) clinical trials and new

programs; e) immunomonitoring in the course of immunotherapy; f) potential interactions of NIBIT with National Cooperative Networks; g) old and new times in cancer immunology.

The scientific and operational activities of the NIBIT are discussed and approved by its Board of Directors. Major ongoing initiatives include: a) to create coordinated working subgroups inside the Network dedicated to specific aspects of cancer bio-immunotherapy (e.g., immunomonitoring, educational, regulatory); b) to design and coordinate clinical studies of cancer bio-immunotherapy. Along this line a new multicenter clinical trial combining high-dose interferon γ and vaccination in melanoma patients will be activated in 2008. In addition to NIBIT-driven clinical studies, pharma-sponsored phase II and III trials are being evaluated to include the active participation of NIBIT groups to their pre-clinical and/or clinical activities; c) to create and activate the NIBIT web-site (www.nibit.org), which will allow access to the diverse activities of the Network, as well as the information on clinical trials of bio-immunotherapy available to cancer patients nationwide; d) to promote the knowledge about cancer bio-immunotherapy among lay people and non-dedicated health professionals. Along this line, different itinerant courses held by NIBIT members are being planned for 2008. Furthermore, an informative booklet on "The use of therapeutic vaccines in cancer" has been prepared and will be distributed by a non-profit Association nationwide; e) to create a coordinated infrastructure of GMP facilities inside the network; f) to establish strong operative interactions with national and European, disease- or approach-oriented, cancer cooperative groups; g) to export the NIBIT "model" at the European level also taking advantage of different European Union initiatives.

In 2007, the research project "*Rete nazionale per studi clinici e di strutture GMP per le bioterapie dei tumori.*

National Network for Clinical Studies and GMP Facilities in Cancer Biotherapy" was approved through the Alleanza Contro il Cancro, providing partial financial support for different activities of the NIBIT described above.

Discussion

We are clearly aware of the multiple difficulties and obstacles still facing the diffusion of the clinical implementation of scientifically-sound cancer bio-immunotherapy strategies at national and European levels. Nevertheless, the ongoing activities of the NIBIT are aimed to contribute to overcome at least part of these obstacles. Along this line, joining the efforts of the NIBIT with existing European networks focused on cancer bio-immunotherapy, and the unrestrained support of The Organization of European Cancer Institutes will certainly make this task less demanding.

References

1. Webb CP, Pass HI: Translation research: from accurate diagnosis to appropriate treatment. *J Transl Med*, 2: 35, 2004.
2. Ioannidis JP: Materializing research promises: opportunities, priorities and conflicts in translational medicine. *J Transl Med*, 2: 5, 2004.
3. Lehmann F, Lacombe D, Therasse P, Eggermont AM: Integration of Translational Research in the European Organization for Research and Treatment of Cancer Research (EORTC) Clinical Trial Cooperative Group Mechanisms. *J Transl Med*, 1: 2, 2003.
4. Pardoll D, Allison J: Cancer Immunotherapy: breaking the barriers to harvest the crop. *Nat Med*, 10: 887-892, 2004.
5. Maio M, Nicolay HJ, Ascierto P, Belardelli F, Camerini R, Colombo MP, Queirolo P, Ridolfi R, Russo V, Anzalone L, Fonsatti E, Parmiani G: The Italian Network for Tumor Biotherapy (NIBIT): getting together to push the field forward. *J Transl Med*, 6: 8, 2008.