



nature publishing group



► **COVER:** 'Patchwork Mice' by Lara Crow, inspired by the Review on p470, which discusses the increasing use of chimeric mice to model the complexities of human cancer.



NICOLA MCCARTHY



GEMMA ALDERTON



SARAH SETON-ROGERS



TERESA VILLANUEVA



MEERA SWAMI

The American Society of Clinical Oncology held its annual meeting at the start of June and reported several findings from a number of clinical trials investigating new targeted agents. Among these was a Phase III trial of an antibody, ipilimumab, which inhibits cytotoxic T lymphocyte antigen 4 (CTLA4). CTLA4 regulates T cell-mediated immune responses and guards against the development of autoimmunity; ipilimumab improved overall survival in patients with progressive melanoma. These results required the collaboration of several international cancer centres, and the trial was statistically powered to address overall survival. However, as we assess more and more targeted agents in clinical trials there is growing concern that the standard progression from Phase I to Phase III is not the best way to rapidly identify the most promising drugs.

On page 514, Johann de Bono and colleagues discuss the need for better-designed clinical trials to minimise the costly failure of new drugs in Phase III trials. They argue that Phase I trials should be smaller and based on solid preclinical data that identify the mechanism of action of a new drug. Moreover, if a drug is likely to work on only a subset of patients with a particular type of cancer, then these should be the patients who are recruited to the early trials, rather than recruiting all cancer patients with advanced disease and then determining in which patients the drug works best, as has been done in the past. However, as de Bono and colleagues acknowledge, not all drug trials can be updated in this way. Ipilimumab, for example, should boost a patient's immune response to several different types of cancer, but why some patients respond and others do not is not yet known. Therefore, standard progression through Phase I–III clinical trials for such agents remains essential to fully understand the mechanism of action.

EDITORIAL OFFICES

LONDON NatureReviews@nature.com

The Macmillan Building,
4 Crinan Street,
London N1 9XW, UK
Tel: +44 (0)20 7843 3620;
Fax: +44 (0)20 7843 3629

CHIEF EDITOR: Nicola McCarthy

SENIOR EDITORS: Gemma Alderton,
Sarah Seton-Rogers

ASSOCIATE EDITOR: Teresa Villanueva

ASSISTANT EDITOR: Meera Swami

COPY EDITOR: Catriona Rodwell

SENIOR COPY EDITOR: Man Tsuey Tse

ART EDITOR: Lara Crow

ART CONTROLLER: Susanne Harris

SENIOR ART EDITORS: Vicky Summersby,
Patrick Morgan

MANAGING PRODUCTION EDITOR:

Judith Shadwell

SENIOR PRODUCTION EDITOR: Simon Fenwick

PRODUCTION CONTROLLER: Natalie Smith

EDITORIAL ASSISTANTS: Jacques Smit,

Laura Corns

WEB PRODUCTION MANAGER:

Deborah Anthony

MARKETING MANAGERS: Tim Redding,

Leah Rodriguez

MANAGEMENT OFFICES

LONDON nature@nature.com

The Macmillan Building, 4 Crinan Street,
London N1 9XW, UK

Tel: +44 (0)20 7833 4000;

Fax: +44 (0)20 7843 4596/7

OFFICE MANAGER: Laura Firman

PUBLISHER: Stephanie Diment

MANAGING DIRECTOR:

Steven Inchcoombe

EDITOR-IN-CHIEF, NATURE PUBLICATIONS:

Philip Campbell

ASSOCIATE DIRECTORS: Jenny Henderson,

Dominic Pettit

EDITORIAL PRODUCTION DIRECTOR:

James McQuat

PRODUCTION DIRECTOR:

Yvonne Strong

DIRECTOR, WEB PUBLISHING:

Dan Pollock

HEAD OF WEB PRODUCTION:

Alexander Thurrell

NEW YORK nature@natureny.com

Nature Publishing Group,

75 Varick Street, 9th floor, New York,
NY 10013-1917, USA

Tel: +1 212 726 9200;

Fax: +1 212 696 9006

CHIEF TECHNOLOGY OFFICER:

Howard Ratner

HEAD OF INTERNAL SYSTEMS DEVELOPMENT:

Anthony Barrera

HEAD OF SOFTWARE SERVICES:

Luigi Squillante

GLOBAL HEAD OF ADVERTISING AND

SPONSORSHIP: Dean Sanderson

HEAD OF NATURE RESEARCH & REVIEWS

MARKETING: Sara Girard

TOKYO nature@natureasia.com

Chiyoda Building 5F, 2-37-1 Ichigayatamachi,

Shinjuku-ku, Tokyo 162-0843, Japan

Tel: +81 3 3267 8751; Fax: +81 3 3267 8746

ASIA-PACIFIC PUBLISHER: Antoine E Bocquet

MANAGER: Koichi Nakamura

ASIA-PACIFIC SALES DIRECTOR:

Kate Yoneyama

SENIOR MARKETING MANAGER:

Peter Yoshihara

MARKETING/PRODUCTION MANAGER:

Takesh Murakami

INDIA SA/12 Ansari Road, Daryaganj,

New Delhi 110 002, India

Tel/Fax: +91 11 2324 4186

SALES AND MARKETING MANAGER, INDIA:

Harpal Singh Gill

Copyright © 2010 Nature Publishing Group

Research Highlight images courtesy of

Getty Images unless otherwise credited.

Printed in Wales by Cambrian Printers

on acid-free paper