

Review

The evolution of phase I trials in cancer medicine: a critical review of the last decade

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Abstract

The advent of targeted therapies, combined with an unsustainable rate of failure in oncology drug development, has resulted in a number of new approaches to clinical trials. Early clinical trials are no exception, with efforts to improve the eventual success rate of late stage trials through evolving phase I trial methodologies, the addition of extensive pharmacodynamic studies, and early adoption of patient selection strategies. Unfortunately, some of these new approaches have met with mixed results. Furthermore, no clear metrics are available to determine whether these designs are more successful than previous strategies. This review examines the evolution of phase I trials and draws upon several examples of strategies that have been successful as well as those that have not, and outlines a pragmatic approach to phase I trials as our understanding of the molecular biology of individual malignancies emerges.

Key words Phase I trial, targeted therapies, pharmacokinetics, pharmacodynamics

In most disciplines of medicine, the objectives of a phase I trial are to determine the maximum tolerated dose (MTD), characterize the pharmacokinetics of the agent in question, and recommend a dose and schedule for further study. In addition, secondary objectives include the determination of whether target engagement can be documented or a therapeutic effect can be observed. These objective(s) and the emphasis on dose determination have served medical research and drug development well for many decades. In contrast to the field of oncology, the majority of these phase I trials have been conducted in a normal healthy volunteer population that endures only limited periods of drug exposure and has no expectation of therapeutic benefit.

In oncology, however, the vast majority of phase I trials are performed within a patient population that has an incurable disease state, and both acute and cumulative toxicities are characterized over several treatment courses. During the era of cytotoxic chemotherapy, it would have been unthinkable to

perform these trials in normal healthy volunteers. Moreover, although therapeutic gain was a low probability, early indications of activity were indeed observed with many agents, some of which led to eventual indications for approval. Furthermore, for the era of cytotoxic chemotherapy, several schedules of administration were concurrently examined in different phase I trials, detailed pharmacokinetics studies were performed, and the recommended dose and schedule was largely based on an analysis of the safety profiles, pharmacokinetics considerations, and preliminary hints of activity. Because the actual target of a cytotoxic agent was not always precisely known, target engagement was largely a speculative argument, with antiproliferative activity, the only pharmacodynamic parameter used to justify dose, in normal tissue (usually neutropenia) and tumor tissue.

In contrast to this past era, the advent of molecular targeted therapies has changed the conduct and expectations of phase I trials. Pharmacodynamic endpoints have greater weight in dose and schedule decisions, and the expectation of objective responses in phase I trials are more prominent. However, three key and recurrent missteps have occurred for many investigational drugs that have limited success in later clinical development. These are best summarized in the following categories: (1) non-validated pharmacodynamic assays that can supplant the use the standard phase I objectives (MTD and pharmacokinetics considerations);

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(2) the presence of a response as an indicator of optimal dose(s); and (3) the presence of the presumed target of the drug as a patient selection criteria. Furthermore, increasing research and development costs along with a high regulatory hurdle for overall survival benefit, have heightened the desire for early and robust evidence of antitumor activity, which may create a disincentive for pursuing potentially important agents and combinations. Each of these themes will be examined and alternative options will be proposed.

Pharmacodynamics, Target Inhibition, and Target Engagement Assays in Phase I Trials of Targeted Therapies: Lessons Learned

Although there is considerable pharmacokinetics expertise in understanding the behavior of a drug product, pharmacodynamics, the effect of a drug on normal and diseased tissue, remains imprecise due to the surrogate nature of the assays. Thus, the results are difficult to interpret. There has been a proliferation of pharmacodynamic endpoints appended to standard phase I trials in the last decade, including tissue biopsies of normal and tumor tissues for protein or RNA expression analysis or target inhibition, dynamic contrast magnetic resonance imaging (DCE-MRI) for angiogenesis inhibition, and positron emission imaging (PET) for tumor inhibition. When subjected to scrutiny, as described in the following examples, these pharmacodynamic studies have not performed admirably, and in some circumstances, may have misled investigators and industry to choose a wrong dose despite evidence to the contrary from the standard phase I trial results.

Gefitinib: good drug, wrong dose and population

Gefitinib is illustrative of several learning opportunities in clinical development. In the phase I trials of this agent, two schedules were initially examined, and the pharmacokinetics behavior and MTD were determined for both the continuous and intermittent dosing schedule^[1,2]. Notably, encouraging antitumor activity was observed in several patients with non-small cell lung cancer (NSCLC) for both schedules^[1,2]. Pharmacodynamic studies included in the daily continuous dosing schedule demonstrated significant inhibition of epithelial growth factor receptor (EGFR) phosphorylation and downstream members of MAPK pathway by immunohistochemistry at early, as well as multiple dose levels^[3]. This led the investigators and authors to propose that dosing at the MTD (750 mg/day) was unnecessary^[3]. A subsequent randomized phase II trial used doses (500 and 250

mg/day) lower than the MTD, with the objective response rate as the benchmark for dose selection^[4,5]. Both dose levels were equally, although marginally active (9%), leading to the conclusion that 250 mg could be moved into phase III trials. In hindsight, the response rate was not a good choice for dose selection because the highly gefitinib-sensitive population of NSCLC patients likely had activating EGFR mutations (discovered post-marketing), and the dose required for stable disease in a less sensitive patient population was unknown but may have indeed been higher^[6]. Phase III trials comparing gefitinib to best supportive care in unselected NSCLC patients were negative, along with a number of other combination trials^[7-10]. In contrast, parallel development of erlotinib, in which the MTD was used throughout phase II and III trials, was ultimately successful, not because of a higher response rate, but likely due to a positive effect on the stable disease rate and altered natural history of disease progression in the treated population^[11,12].

This dose and population example raises some interesting yet unanswered questions. Why did the dose not prove effective for the population as a whole if early pharmacodynamic markers indicated target inhibition? Although inhibition was demonstrated in the assays used (immunohistochemistry), was this assay sufficiently sensitive to detect retained and still important EGFR activity? Also, there was an absence of information regarding the optimal inhibition rate to indicate efficacy in phase III studies—should it have been 90%, 99%, or 99.9% inhibition?

To address these questions, one must examine the requirements for a validated pharmacodynamic test. To be validated in drug development, the pharmacodynamic test must demonstrate a perturbation due to therapeutic intervention, and a change that must be reproducible and not subject to disparate, random, or hard to explain variability. The test must also reliably predict a positive or negative outcome for therapeutic intervention. Because the outcome necessary for most new drugs in oncology to meet regulatory approval is an improvement in overall survival, the only way to meet the last criterion and to validate a pharmacodynamic marker would be to prove that marker predicts overall survival—something very hard to accomplish. The absence of a validated pharmacodynamic biomarker should not, in itself, stop the use or development of these markers during the course of clinical development, but should merely frame the discussion of their relative merits for dose and/or patient selection.

Further confounding the gefitinib story, the absence of an identified population that would attain all the response benefits at the time of the randomized phase II trial led to false assumptions that dose did not matter, resulting in the utilization of the lower dose in the phase III trial comparing gefitinib with standard best supportive

care^[7]. In retrospect, the reason that the two doses were equivalent in response rate was the presence of a mutation within the tumors of a NSCLC subpopulation^[6]. For these patients, dose may not have been important. However, it is incorrect to assume that dose may not be important for patients with other, less sensitive NSCLC.

PTK787: did a non-validated imaging endpoint outweigh dose and pharmacokinetics data?

The multi-targeted tyrosine kinase inhibitor of vascular endothelial growth factor receptor 2 (VEGFR2), PTK787, underwent a standard phase I design with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), proposed at the time to be a novel pharmacodynamic endpoint. Although a MTD was determined for PTK787 and the pharmacokinetics profile indicated a rapid systemic clearance, the DCE-MRI data suggested that a lower dose could result in decreased tumor blood flow^[13,14]. Ultimately, a lower dose and less frequent schedule (for example, twice per day) of this oral angiogenesis inhibitor was adopted for the randomized study in front-line metastatic colorectal carcinoma comparing FOLFOX combined with PTK787 to FOLFOX alone, mirroring the successful design for bevacizumab approval in colorectal cancer^[15]. Unfortunately, the endpoint of an improvement in overall survival was not achieved in this study^[16].

Retrospectively, several issues may have contributed to the failed phase III trial. PTK787 is rapidly cleared, and therefore, sustained inhibition of tumor angiogenesis may not have been achieved with a once- or twice-daily schedule. The dose for optimal inhibition may also have been inferior, due to the misleading information gained from the positive pharmacodynamic effects of PTK787 on the DCE-MRI images. A logical question in this regard is whether DCE-MRI is a validated pharmacodynamic marker. DCE-MRI appeared to meet the first criteria of validated markers, showing that perturbation occurred due to drug effect and that the results were potentially reproducible from usual day-to-day variation (the investigators never demonstrated the variability of the test in a control situation). However, the last of the aforementioned criteria was not met, as DCE-MRI alterations did not predict ultimate success in the only endpoint that mattered for the randomized study (overall survival). The conclusion is that DCE-MRI is a surrogate endpoint for drug effect but not otherwise validated against the one endpoint that is meaningful in oncology. The standard phase I trial endpoints of MTD, pharmacokinetics characterization, and selection of a recommended dose and schedule should have prevailed compared to decisions made based upon DCE-MRI studies. This has important implications for other pharmacodynamic markers currently being developed; they must predict ultimate success in phase III trial to be truly validated—a

non-trivial challenge.

Since the early development and subsequent failure of PTK787, many investigational angiogenesis inhibitors have included DCE-MRI analysis as part of the early development process. To date, no agent with a positive effect on DCE-MRI in early clinical trials that affected dose has yielded later success in regulatory approval. Those agents that did succeed and reach regulatory approval following successful randomized studies, including bevacizumab, sorafenib, and sunitinib, had the dose and schedule determined using conventional phase I design without direction from a DCE-MRI pharmacodynamic endpoint.

Positron emission tomography

Positron emission tomography (PET) scans are increasingly being incorporated into early clinical trials. Although frequently used, there appears little evidence to support the routine adoption of this imaging modality as a pharmacodynamic endpoint, as it appears to have only limited advantages compared to conventional imaging. The oft-cited example of PET scans providing useful information in drug development was the development of imatinib and sunitinib in gastrointestinal tumors (GIST)^[16]. Nonetheless, both drugs had already met proof-of-concept in other disease indications (chronic myelogenous leukemia and renal cell carcinoma, respectively), so the utility of PET in phase I development is open to debate. A more common outcome in early clinical trials is a change in PET standard uptake values (SUV) post-treatment without a corresponding change in measurements in CT scan. This result gives little direction to investigators. Furthermore, the less common circumstance that a PET response is observed before a later confirmed CT response raises the question of whether the PET response merely indicates what will later be determined with CT anyway. Lastly, as most phase I trials include low doses that are unlikely to have either a therapeutic or biological effect, the performance of PET scans is hard to justify based on cost and the potential for misleading SUV variability for the majority of populations enrolled in phase I trials. Based on this analysis, PET studies should be viewed as an investigational, non-validated and an expensive tool in phase I trials. Clear objectives for their use in clinical trials and metrics to assess their value should be defined before this surrogate endpoint is used for dose selection.

It must be clearly stated that these aforementioned arguments in no way diminish the use of conventional PET or PET CT in validated settings such as monitoring response in non-Hodgkin's lymphoma, the detection of metastases in early workup for potentially curative surgery, or as a modality that may decide effective therapy. These indications have an extensive literature to support their use.

Molecularly targeted therapy: only with an improved understanding of molecular hierarchy may we improve success

Despite an impressive list of investigational targeted therapies to known receptors and signal transduction pathway members, the ability to determine which patients will respond in early clinical trials remains elusive. Initially, tumor biopsies were interrogated for the presence or absence of the target or activation of the specific pathway. Unfortunately, this area of scientific enquiry did not yield results and, to some extent, created unintended consequences. The EGFR-targeting antibody, cetuximab, was developed with activity noted in colorectal carcinoma^[17,18]. Detection of the target EGFR frequently accompanied early clinical studies, with levels of EGFR expression or activated (phosphorylated) EGFR hypothesized to be predictive of response though never confirmed in controlled studies. Following the regulatory approval of cetuximab in colorectal carcinoma, some third party payers required detection of EGFR in tumor specimens for reimbursement, thereby restricting the agent from some patients^[19]. Ultimately, EGFR expression was found not have any predictive value for cetuximab efficacy, whereas an apparently unrelated genetic alteration, mutation of KRAS, predicted resistance to cetuximab therapy^[20-22]. To date, a positive-predictive marker for response has not been defined^[23].

This case illustrates the difficulty with several targeted therapies currently being developed. Although intuitive that the target be present for therapeutic benefit, this is not always the case^[20]. In addition, pathway activation may be part of a constellation of events secondary to upstream molecular events, and inhibition of one target alone may have little effect. Lastly, some events are hypothesized to have a greater impact than others; sometimes described as the “RASness” of a genotype, indicating that drugs targeting other molecular events such as PTEN deletions and PIK3Ca mutations have little impact in the presence of an activating RAS mutation.

This uncertainty calls into question some designs for patient selection for phase I trials when the molecular genetic hierarchy is unknown. Does a BRAF V600E mutation in colorectal cancer have the same impact in melanoma? Preliminary clinical data with investigational RAF inhibitors suggests that they have little activity in colorectal carcinomas with BRAF V600E but profound activity in a melanoma population with the same molecular alteration^[24]. Furthermore, does the presence or absence of a PTEN deletion influence the response to a MEK or BRAF inhibitor? Emerging data appear to suggest this finding, but further scrutiny will be required. These two questions illustrate that an absence of a thorough understanding of the hierarchy and relationships of discrete molecular genetic events may

lead to the misinterpretation of the results of clinical studies and potentially miss indications that benefit from therapy.

Two successful targeted therapies offer a word of caution about patient selection based upon a premature assessment of the target. Sorafenib was originally presumed to be an inhibitor of RAF signaling. If patients had been selected based upon RAF status, such as the activating mutation of V600E in melanoma, the drug would never have succeeded because no significant activity was found in this indication. Rather, the inhibitory effects of sorafenib on VEGFR2 ultimately led to a successful strategy in renal cell and hepatocellular carcinoma^[25,26]. Similarly, crizotinib was initially thought to primarily inhibit c-MET^[27]. If selection in the phase I trial had been confined to patients with activating mutations or amplifications of c-MET, the remarkable activity in NSCLC patients with EML4-ALK fusion may have been missed.

A Path Forward

Although our understanding of the molecular biology of numerous malignancies has improved, we are far from demonstrating a complete or sophisticated understanding of existing genetic changes and their inter-relationships and network functions, as well as the hierarchy amongst multiple genetic alterations. Recently paired tumor and normal tissue analysis in NSCLC convincingly illustrates that our view of drug development in this disease may be embarrassingly naïve, as we may be treating patient tumors that possess more than 30–40 major genetic alterations, while developing and celebrating the success of agents that target a single genetic change^[28]. This recent work puts into perspective the magnitude of the problem and naïvety of the expectation that any single agent can routinely demonstrate responses in early clinical trials. In fact, it implicates the opposite outcome will occur. Individual targeted therapies will fail to demonstrate significant antitumor activity even if one of the catalogued mutations is present, unless this genetic change has significant proliferation potential alone (an outlier perhaps). Therefore, single genetic changes are not yet justified as routine patient selection criteria in phase I trials. The implication, based upon the aforementioned conclusion, is that we must intensify our efforts to develop safe combinations in phase Ib trials, and it is with these combinations that we will have significant impact in selected populations with most of the common tumors.

To accomplish rational drug development in the coming decade, the focus in phase I trials must remain on the determination of safety and defining a recommended dose and schedule. The characterization of the molecular genetics of the few patients whose tumors respond should be intensified to explore these

infrequent opportunities and determine unique features that may predict both future indications and patient selection. Expansion cohorts in selected patients at the end of phase I trials may, in some circumstances, abrogate the need for phase II trials. This strategy represents an innovative and practical solution to the rising cost and time in clinical development and has been successfully deployed with some agents^[29]. In the

next decade, as widespread molecular screening of cancer patients for common mutations occurs, patient pre-selection for participation on phase I trials will no doubt improve and perhaps increase the likelihood of observed responses.

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References

- [1] Ranson M, Hammond LA, Ferry D, et al. ZD1839, a selective oral epidermal growth factor receptor-tyrosine kinase inhibitor, is well tolerated and active in patients with solid, malignant tumors: results of a phase I trial [J]. *J Clin Oncol*, 2002,20(9):2240–2250.
- [2] Herbst RS, Maddox AM, Rothenberg ML, et al. Selective oral epidermal growth factor receptor tyrosine kinase inhibitor ZD1839 is generally well-tolerated and has activity in non-small-cell lung cancer and other solid tumors: results of a phase I trial [J]. *J Clin Oncol*, 2002,20(18):3815–3825.
- [3] Baselga J, Rischin D, Ranson M, et al. Phase I safety, pharmacokinetic, and pharmacodynamic trial of ZD1839, a selective oral epidermal growth factor receptor tyrosine kinase inhibitor, in patients with five selected solid tumor types [J]. *J Clin Oncol*, 2002,20(21):4292–4302.
- [4] Fukuoka M, Yano S, Giaccone G, et al. Multi-institutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer (The IDEAL 1 Trial) [J]. *J Clin Oncol*, 2003,21(12):2237–2246.
- [5] Wolf M, Swaisland H, Averbuch S. Development of the novel biologically targeted anticancer agent gefitinib: determining the optimum dose for clinical efficacy [J]. *Clin Cancer Res*, 2004,10(14):4607–4613.
- [6] Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib [J]. *N Engl J Med*, 2004,350(21):2129–2139.
- [7] Thatcher N, Chang A, Parikh P, et al. Gefitinib plus best supportive care in previously treated patients with refractory advanced non-small-cell lung cancer: results from a randomised, placebo-controlled, multicentre study (Iressa Survival Evaluation in Lung Cancer) [J]. *Lancet*, 2005,366(9496):1527–1537.
- [8] Kelly K, Chansky K, Gaspar LE, et al. Phase III trial of maintenance gefitinib or placebo after concurrent chemoradiotherapy and docetaxel consolidation in inoperable stage III non-small-cell lung cancer: SWOG S0023 [J]. *J Clin Oncol*, 2008,26(15):2450–2456.
- [9] Herbst RS, Giaccone G, Schiller JH, et al. Gefitinib in combination with paclitaxel and carboplatin in advanced non-small-cell lung cancer: a phase III trial—INTACT 2 [J]. *J Clin Oncol*, 2004,22(5):785–794.
- [10] Giaccone G, Herbst RS, Manegold C, et al. Gefitinib in combination with gemcitabine and cisplatin in advanced non-small-cell lung cancer: a phase III trial—INTACT 1 [J]. *J Clin Oncol*, 2004,22(5):777–784.
- [11] Cappuzzo F, Ciuleanu T, Stelmakh L, et al. Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: a multicentre, randomised, placebo-controlled phase 3 study [J]. *Lancet Oncol*, 2010,11(6):521–529.
- [12] Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer [J]. *N Engl J Med*, 2005,353(2):123–132.
- [13] Morgan B, Thomas AL, Drevs J, et al. Dynamic contrast-enhanced magnetic resonance imaging as a biomarker for the pharmacological response of PTK787/ZK 222584, an inhibitor of the vascular endothelial growth factor receptor tyrosine kinases, in patients with advanced colorectal cancer and liver metastases: results from two phase I studies [J]. *J Clin Oncol*, 2003,21(21):3955–3964.
- [14] Thomas AL, Morgan B, Horsfield MA, et al. Phase I study of the safety, tolerability, pharmacokinetics, and pharmacodynamics of PTK787/ZK 222584 administered twice daily in patients with advanced cancer [J]. *J Clin Oncol*, 2005,23(18):4162–4171.
- [15] Tyagi P. Vatalanib (PTK787/ZK 222584) in combination with FOLFOX4 versus FOLFOX4 alone as first-line treatment for colorectal cancer: preliminary results from the CONFIRM-1 trial [J]. *Clin Colorectal Cancer*, 2005,5(1):24–26.
- [16] Blanke CD, Demetri GD, von Mehren M, et al. Long-term results from a randomized phase II trial of standard- versus higher-dose imatinib mesylate for patients with unresectable or metastatic gastrointestinal stromal tumors expressing KIT [J]. *J Clin Oncol*, 2008,26(4):620–625.
- [17] Fracasso PM, Burris H 3rd, Arquette MA, et al. A phase 1 escalating single-dose and weekly fixed-dose study of cetuximab: pharmacokinetic and pharmacodynamic rationale for dosing [J]. *Clin Cancer Res*, 2007,13(3):986–993.
- [18] Taberner J, Van Cutsem E, Diaz-Rubio E, et al. Phase II trial of cetuximab in combination with fluorouracil, leucovorin, and oxaliplatin in the first-line treatment of metastatic colorectal cancer [J]. *J Clin Oncol*, 2007,25(33):5225–5232.
- [19] Ensinger C, Sterlacci W. Implications of EGFR PharmDx kit for cetuximab eligibility [J]. *Expert Rev Mol Diagn*, 2008,8(2):141–148.
- [20] Chung KY, Shia J, Kemeny NE, et al. Cetuximab shows activity in colorectal cancer patients with tumors that do not express the epidermal growth factor receptor by immunohistochemistry [J]. *J Clin Oncol*, 2005,23(9):1803–1810.
- [21] Allegra CJ, Jessup JM, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: testing for KRAS gene mutations in patients with metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy [J]. *J Clin Oncol*, 2009,27(12):2091–2096.
- [22] Ogino S, Meyerhardt JA, Irahara N, et al. KRAS mutation in stage III colon cancer and clinical outcome following intergroup trial CALGB 89803 [J]. *Clin Cancer Res*, 2009,15(23):7322–7329.
- [23] Laurent-Puig P, Cayre A, Manceau G, et al. Analysis of PTEN, BRAF, and EGFR status in determining benefit from cetuximab therapy in wild-type KRAS metastatic colon cancer [J]. *J Clin Oncol*, 2009,27(35):5924–5930.
- [24] Flaherty KT, Puzanov I, Kim KB, et al. Inhibition of mutated, activated BRAF in metastatic melanoma [J]. *N Engl J Med*, 2010,363(9):809–819.

- [25] Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma [J]. *N Engl J Med*, 2007,356 (2):125–134.
- [26] Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma [J]. *N Engl J Med*, 2008,359 (4): 378–390.
- [27] Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer [J]. *N Engl J Med*, 2010,363(18):1693–1703.
- [28] Lee W, Jiang Z, Liu J, et al. The mutation spectrum revealed by paired genome sequences from a lung cancer patient [J]. *Nature*, 2010,465(7297):473–477.
- [29] Infante JR, Fecher LA, Nallapareddy S, et al. Safety and efficacy results from the first-in-human study of the oral MEK 1/2 inhibitor GSK1120212 [J]. *J Clin Oncol*, 2010,28(suppl): 15s.



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January 6–7, 2012 in Sun Yat-sen University Cancer Center, Guangzhou

This symposium, hosted by Sun Yat-sen University Cancer Center and organized in collaboration with the University of Texas MD Anderson Cancer Center, aims to address various topics from basic to translational and clinical research on head and neck cancer with a particular focus on nasopharyngeal carcinoma. The program will include a multi-disciplinary approach with international specialists, from both the United States and China, in surgery, radiation oncology and medical oncology. In addition with scientists from Sun Yat-sen University Cancer Center, speakers from various leading cancer institute in China will be convened, namely, the Cancer Institute and Hospital of Chinese Academy of Medical Sciences and Peking Union Medical College (CAMS), Tianjin Medical University Cancer Institute and Hospital (TMUCIH), Fudan University Shanghai Cancer Center (FUSCC) and Chinese University of Hong Kong (CUHK).

Keynote Speakers and Symposium Chairpersons

Dr. Ronald A. DePinho

President, The University of Texas MD Anderson Cancer Center
Internationally recognized for basic and translational research in cancer, aging and age-associated degenerative disorders, is the fourth full-time president of The University of Texas MD Anderson Cancer Center.

Dr. Yi-Xin Zeng

President, Sun Yat-sen University Cancer Center
President of Sun Yat-sen University Cancer Center since 1997, his research focuses on the characterization of the pathogenesis mechanisms and gene therapies for nasopharyngeal carcinoma which is a prevalent malignancy in South China.

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Professor, Department of Clinical Cancer Prevention

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