

Institute of Medicine Comparative Oncology Workshop

Anne Keane, PA-C, JD

The opinions expressed in this presentation and on the following slides are solely those of the presenter and not necessarily those of my current or former employers.

Background

- Director of Regulatory Affairs, Achaogen Pharmaceuticals-antibiotics for MDR gram negative infections
- Various roles in academic clinical research and industry drug development since 1982
- Oncology drug development between 2008 - 2014
- Previously Director, Global Oncology Regulatory Affairs at Genentech Roche and Team Leader for the Comparative Oncology Initiative Team*
- Parent of a 12.5 yo canine cancer survivor – 5 months post surgery and radiation for hind limb soft tissue sarcoma

Current challenges in cancer drug development

- Oncology drug development is extremely expensive, crowded and fiercely competitive
 - 800+ oncology compounds in pipeline 2010; 576 in late (Phase II-III) clinical studies in 2014
 - ~5,000 ongoing oncology drug studies
 - 3-5 molecules/receptor/company, few-15 competitors in same space
 - In intense competition for development dollars, time to market critical
 - 1 month delay to market may = millions - hundreds of millions/month
 - Small populations may not support multiple agents
 - Slow patient recruitment and trial bureaucracy adds time and cost pressure
 - Average time to complete oncology trial 70% longer than planned
 - Particular problem for pediatric studies – EU Pediatric Regulation/PREA required studies, but numbers issue (annual US new cancer diagnoses/year = 1,658,370 of which only 16,000 are new pediatric cancers)
 - 70% of pharma cos say recruitment is a #1 challenge in pediatric drug development)

What does this mean for oncology drug development?

- Accelerated development: traditional Phase I → Phase II → Phase III paradigm is quickly being replaced with Phase I/II → Phase III or Phase I → Phase III
- Role of Phase I trials has expanded –
 - Identify target population for pivotal trials -
 - Current nonclinical models not predictive enough
 - Phase I trials generally still recruit broad advanced solid tumor populations – dilutes the ability of trial to identify the correct population
 - Provide justification for Phase III dose and schedule
 - Phase I response results may determine whether compound progresses – need extraordinary results
- Even drugs that progress do so at high development risk because the critical (Phase II) refinement work (patient population, dose, dosing regimen) is shortchanged

Clinical development success rates for investigational drugs

Table 3 Comparison of our study with previous drug development success rate studies

	This study (2013) all indications		This study (2013) lead indications		DiMasi <i>et al.</i> ⁶ lead indications		Kola <i>et al.</i> ⁸ lead indications		Abrantes-Metz <i>et al.</i> ⁹ lead indications	
	Phase success	Phase LOA	Phase success	Phase LOA	Phase success	Phase LOA	Phase success	Phase LOA	Phase success	Phase LOA
Phase 1 to phase 2	64.5%	10.4%	66.5%	15.3%	71%	19%	68%	11%	80.7%	NA
Phase 2 to phase 3	32.4%	16.2%	39.5%	23.1%	45%	27%	38%	16%	57.7%	NA
Phase 3 to NDA/BLA	60.1%	50.0%	67.6%	58.4%	64%	60%	55%	42%	56.7%	NA
NDA/BLA to approval	83.2%	83.2%	86.4%	86.4%	93%	93%	77%	77%	NA	NA
LOA from phase 1 ^a		10.4%		15.3%		19%		11%	26.4% ^c	NA
Number of drugs in sample advanced or suspended ^b	5,820		4,736		1,316		NA		2,328	
Dates of source data (duration)	2003–2011 (9 years)				1993–2009 (17 years)		1991–2000 (10 years)		1989–2002 (14 years)	
Number of companies	835				50		10		NA	

^aProbability of FDA approval for drugs in phase 1 development. ^bTotal number of transitions used to calculate the success rate (the *n* value noted in the text). ^cAbrantes-Metz, *et al.*⁹ reported 26.4% from phase 1 to phase 3. If we were to conservatively apply the 83.2% NDA/BLA success rate found in this study, Abrantes-Metz would yield the highest LOA from phase 1 (21%). NA, data not available.

Clinical development success rates for investigational drugs

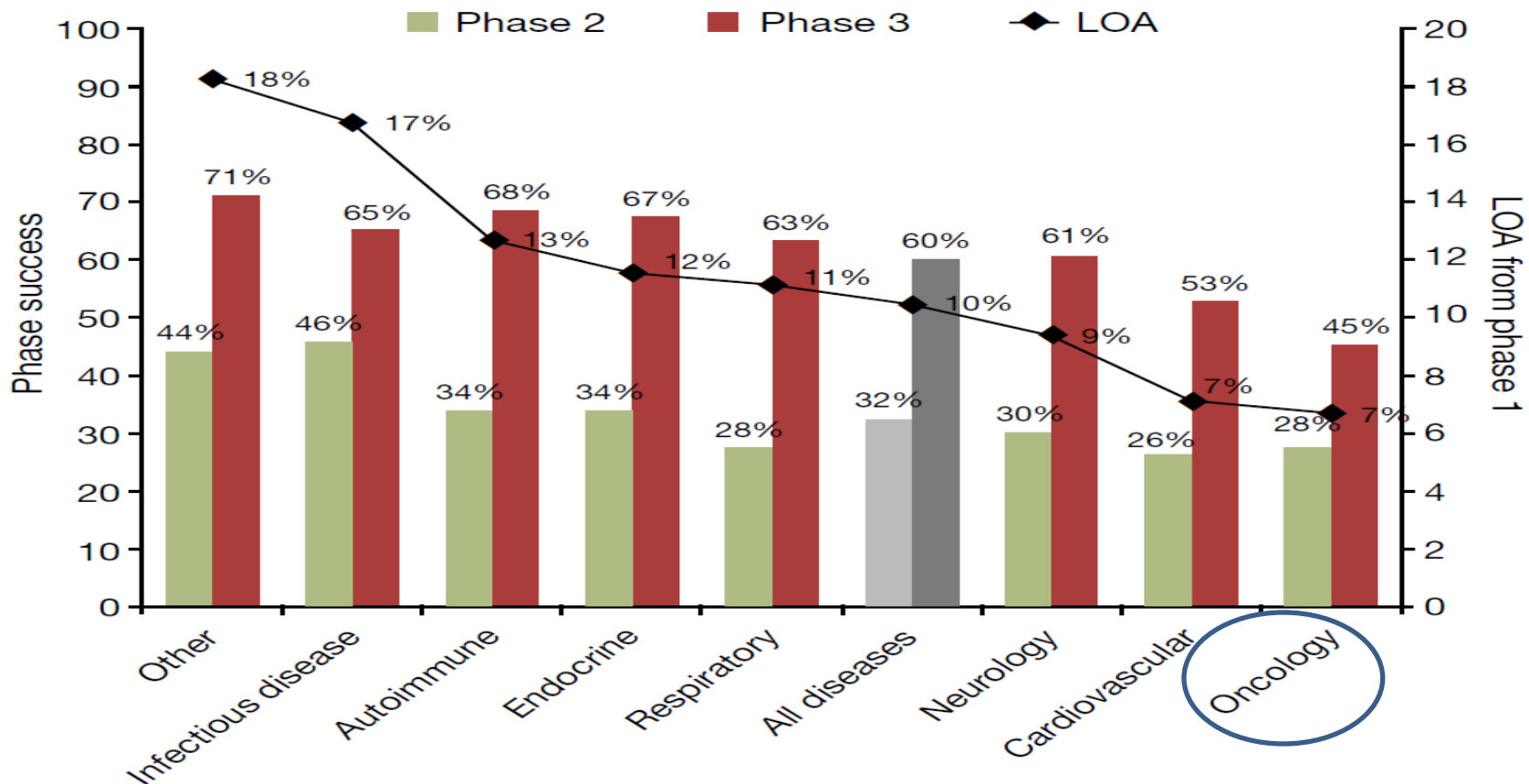


Figure 2 Phase success and LOA from phase 1 by disease for all indications. The bars represent phase 2 and phase 3 success rates and the line represents LOA from phase 1.

How can studies in companion animals help?

Iterative development utilizing all the data from canine and human studies

- Identify and credential canine models early so that canine cell lines can be added to screening panels for all compounds
 - Common effort - Can't afford the time or expense of duplicating efforts at every pharma co
- Select the best compound to advance into the clinic
- Thoroughly interrogate PK/PD and identify PD and imaging endpoints that can be used to inform human dosing
- Identify possible safety signals early to permit thorough evaluation and mitigation strategies
- Prioritize the most promising combinations to advance into patients
- Rationale selection of most promising compounds to advance into pediatric trials

How did we introduce Comparative Oncology into Genentech Development

- Presentation to the highest development committee in the company
- Requested and received a Comparative Oncology cross-functional team, with project management support
 - Mandate- Evaluate the comparative oncology opportunity and design and execute pilot studies in cooperation with molecule teams
- 2-day collaborative project proposal workshop (CSU, NCI)
 - 5 teams came with proposals
 - 1 eliminated (lack of clear objectives, but may be coming back)
 - 4 moved forward:
 - 2 research molecules: one program d/ced due to safety, one recently completed
 - 1 early development molecule - on hold, issues with getting access to canine version of competitor
 - 1 new indication for an approved molecule- ongoing
- Ongoing efforts to educate and identify new collaborations
 - Monthly speaker series (Jaime Modiano, Pete Dickinson)

What are the barriers the team faced and how were/can they be addressed?

Lack of familiarity with veterinary medicine

- Team-based approach to incorporation of comparative approach into development
- Continuous education
- Speaker series – NCI, academic vet researchers
- Forge connections and collaborations with NCI and academic vet schools
- Publish in human medicine journals and present at national human medicine meetings
- Support for academic veterinary-human medicine collaborations

Logistics

- Contracts, MTA process is too slow
- Dedicated legal representatives
- Prospective nonexclusive licenses
- Renegotiation of each contract

Fear of safety events that derail program

- Continuous education
- Enlist senior safety representatives as members of team
- Recast as opportunity to de-risk and mitigate

Perception of lack of regulatory guidance

- Clin Cancer Res, 2009;15(18):5671–7
Guiding the Optimal Translation of New Cancer Treatments From Canine to Human Cancer Patients

Ability to recruit adequate numbers

Human oncology – only 10% of oncologists have ever enrolled a patient

- Huge geographic mismatch
- 85% of patients get care locally
- Engage local oncologists as community investigators

What is the future?

- Pharma will come around but it will be slow and it will be piecemeal
- Waiting for that to happen will waste a lot precious time and resources
- Is there another option?

List of highest funded crowdfunding projects

From Wikipedia, the free encyclopedia

This is an incomplete list of the most well-funded crowdfunding projects, either successful or not.

Rank	Project	Category	Platform	Campaign end date	Campaign target	Amount raised	Notes	References
1	<i>Star Citizen</i>	Video game	Kickstarter, Independent	Ongoing	\$500,000	\$83,002,764	Space combat video game from Chris Roberts, designer of <i>Wing Commander</i> . It is the largest crowd-funded project of any genre with over 898,000 backers. Listed on December 2014 at more than \$65,300,000 as a Guinness World Record. Of the total amount, \$6,238,563 were raised on Kickstarter and Roberts' own website on November 19, 2012.	[1][2][3][4][5][6]
2	<i>Pebble Time</i>	Smartwatch	Kickstarter	Mar 27, 2015	\$500,000	\$20,338,986	The Pebble Time is the third generation version of the smartwatch called the Pebble Watch. The Pebble Watch itself was one of the highest backed project on Kickstarter.	[7]
3	<i>Ethereum</i>	Cryptocurrency	Bitcoin, Independent	Sept 2, 2014	-	\$18,439,086	Ethereum is a decentralized publishing platform featuring stateful user-created digital contracts and a Turing-complete contract programming language.	[8][9]
4	<i>Coolest Cooler</i>	Product Design	Kickstarter	Aug 29, 2014	\$50,000	\$13,285,226	Portable 60 quart cooler designed by Ryan Grepper that contains a battery powered rechargeable blender, waterproof Bluetooth speaker, USB charger, cutting board, plates, among other features.	[10][11]
5	<i>Ubuntu Edge</i>	Smartphone	Indiegogo	Aug 21, 2013	\$32,000,000	\$12,814,196	The Ubuntu Edge was a proposed "high concept" smartphone announced by Canonical Ltd. on 22 July 2013. It had the highest target of any crowdfunded project to date, \$32,000,000 over a one-month campaign.	[12]
6	<i>Flow Hive</i>	Beehive	Indiegogo	Apr 19, 2015	\$70,000	\$12,174,187	Harvesting honey is easier on the beekeeper and so much easier on the bees.	[13][14]
7	<i>Pebble (watch)</i>	Smartwatch	Kickstarter	May 18, 2012	\$100,000	\$10,266,845	E-Paper smartwatch. Second highest funded project on Kickstarter. Shipping to backers began on 23 Jan 2013.	[15][16]
8	<i>Exploding Kittens</i>	Card game	Kickstarter	Feb 19, 2015	\$10,000	\$8,782,571	Card game featuring exploding kittens, designed by Elan Lee, Matthew Inman, and Shane Small. The project hit its primary goal in only 8 minutes, exceeded \$100,000 (10x its goal) in less than one hour, \$1,000,000 (100x its goal) in less than 8 hours, and \$2,000,000 (200x its goal) in just over 24 hours. On January 27, 2015, just seven days after the project opened, it passed 106,000 backers, making it the most backed Kickstarter to date.	[17][18][19]

THANK YOU!



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