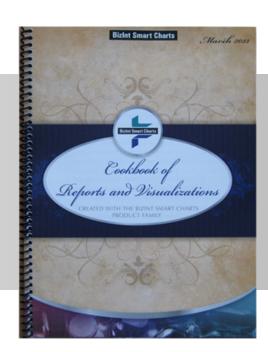


Developing a "Cookbook" of Reports & Visualizations for Drug Target CI

February 18, 2014 Pharma CI Europe, Barcelona

Diane Webb, President, BizInt Solutions John Willmore, VP, BizInt Solutions



Commercial databases support drug target CI

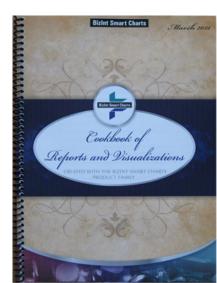
- Drug pipeline, clinical trial, and patent databases provide key ingredients for target analysis.
- Each has strengths and weaknesses in both coverage and content.

You must exploit multiple sources to create information-rich reports with depth of insight.

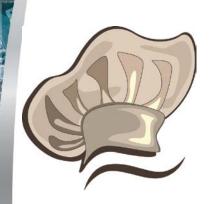
Final slides at: www.bizint.com/slides

Exploiting these sources presents challenges.

- The Cookbook contains a collection of tantalizing recipes to create accurate and appealing visuals from these raw ingredients.
- The recipes will serve you well, whether presenting to a group or for your own analysis.
- Substitute ingredients as needed to answer *your* business questions.



PARP- a target in three courses



Today, we will investigate PARP inhibitors (poly ADP-ribose polymerase) – an example of a target that seemed promising, failed in early trials, and is now undergoing a revival.

What are *your* current Top Targets?

PARP- a target in three courses



menu

February 18, 2014

Appetizer

visualizing the pipeline landscape

Entrée

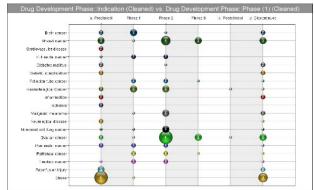
a selection of clinical trial timelines

Dessert

a foray into Chinese patents

Appetizer – Visualizing the Pipeline Landscape

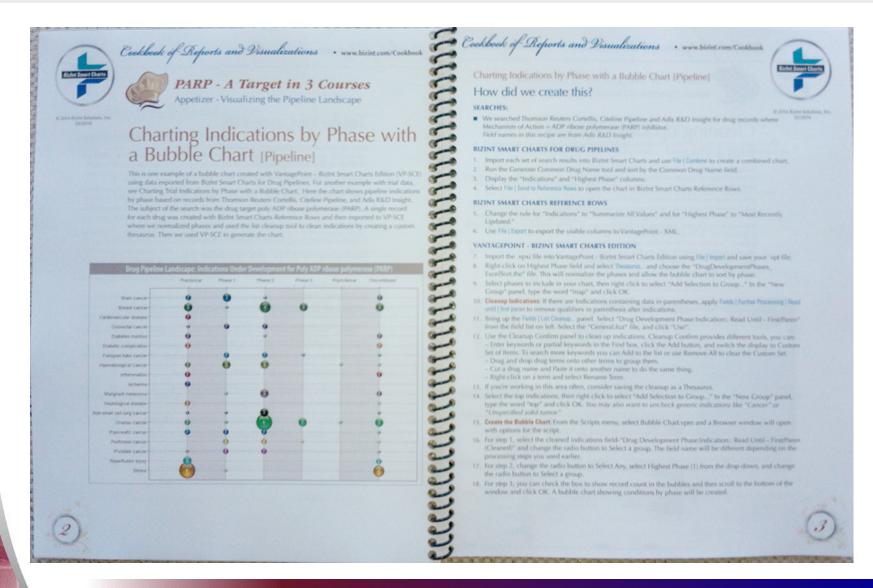
The Challenge:



What does the PARP inhibitor development pipeline look like in 2014?

Background: Excitement around PARP inhibitors, past and present, stemmed from the prospect that inhibition of the enzyme would exploit a pre-existing weakness in cancer cells, triggering their self-destruction while avoiding collateral damage. A series of setbacks almost caused the demise of a very promising class of compounds called PARP Inhibitors (poly (ADP-ribose) polymerase). Today a few companies are beginning pivotal Phase III trials of these agents in breast and ovarian cancer.

Appetizer – The Recipe



Appetizer – Choose your ingredients



- Drug pipeline databases provide detailed information on drugs in development worldwide.
- For this recipe, we will use Thomson Cortellis,
 Citeline Pipeline, and Adis R&D Insight.
- These databases can be searched by targets (e.g. PARP) and each provide a variety of useful information about drug compounds.

Appetizer – Mise en Place/ Prep Work



- Searched 3 pipeline databases:
 - Thomson Reuters Cortellis 45 records
 - Citeline Pipeline 67 records
 - ADIS R&D Insight 47 records
- Searched for inhibitors of poly ADP-ribose polymerase (PARP) for all phases of development including withdrawn, discontinued, suspended and no development reported.

Appetizer – Recipe at a glance

- BizInt Smart Charts for Drug Pipelines
 Import results from each database and combine
- BizInt Smart Charts Reference Rows
 Create a single row and summarize indications for each drug
- VantagePoint Smart Charts Edition
 - Normalize phases
 - Clean up indications
 - Create a Bubble Chart

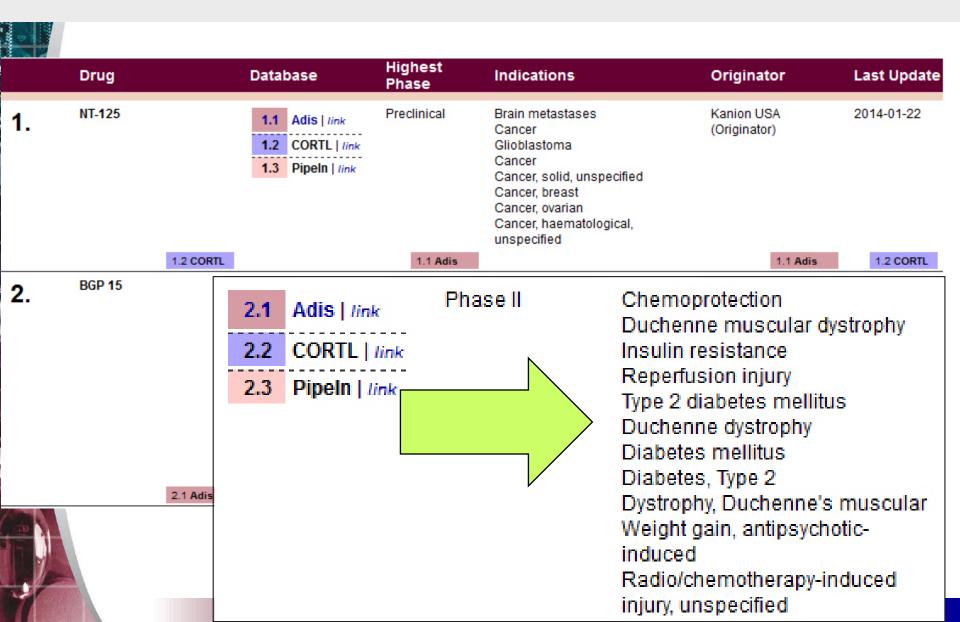
Appetizer – Combining the ingredients

	Drug	Common Drug Name	Database	Highe	est Phase	Indications		Originator	Last Update						
1	Research programme: cancer therapeutics - NewGen/Kanion	NT 125	Adis R&D Preclinical Insight		inical	Brain metastases Cancer Glioblastoma	К	anion USA (Originator)	2013-11-27						
2	NT-125	NT 125	Thomson Reuters Cortellis	Disco	overy	Cancer		angsu Kanion harmaceutical Co Ltd	2014-01-22						
	NT-125	NT 125	Citeline Pipeline	Precli	inical	Cancer, solid, unspecified	N	ewGen Therapeutics	2013-07-11						
Α	dis R&D	Phas	se II		Che	moprotection		_							
Ir	nsight				Duchenne muscular dystrophy										
					Insulin resistance										
					Reperfusion injury										
					Type 2 diabetes mellitus										
C	iteline Pipelir	ne Phas	se II		Diabetes, Type 2										
						Dystrophy, Duchenne's muscular									
					Weight gain, antipsychotic-induced										
					Radio/chemotherapy-induced injury, unspecified										
T	homson	Phas	e 2 Clini	cal	Duchenne dystrophy										
R	leuters				Diat	etes mellitus									
C	ortellis														

Appetizer – Recipe at a glance

- BizInt Smart Charts for Drug Pipelines
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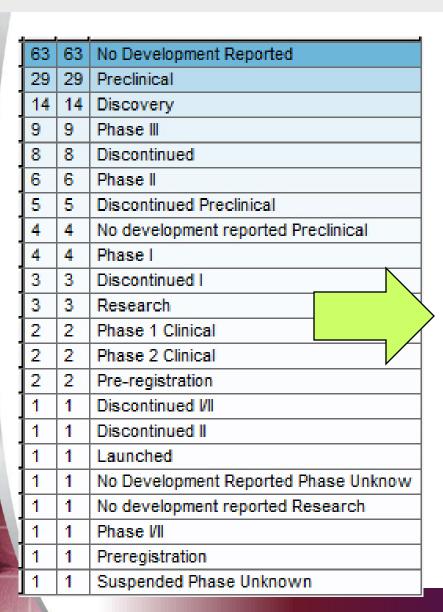
Appetizer – Summarizing indications



Appetizer – Recipe at a glance

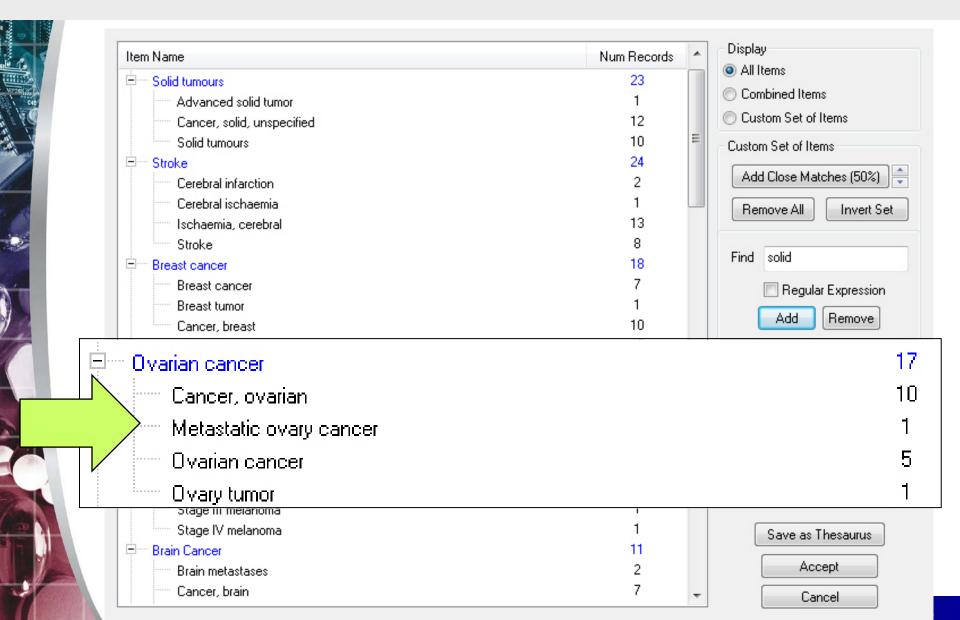
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 Create a single row and summarize indications for each drug
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Appetizer – Use VP-SCE to normalize phases



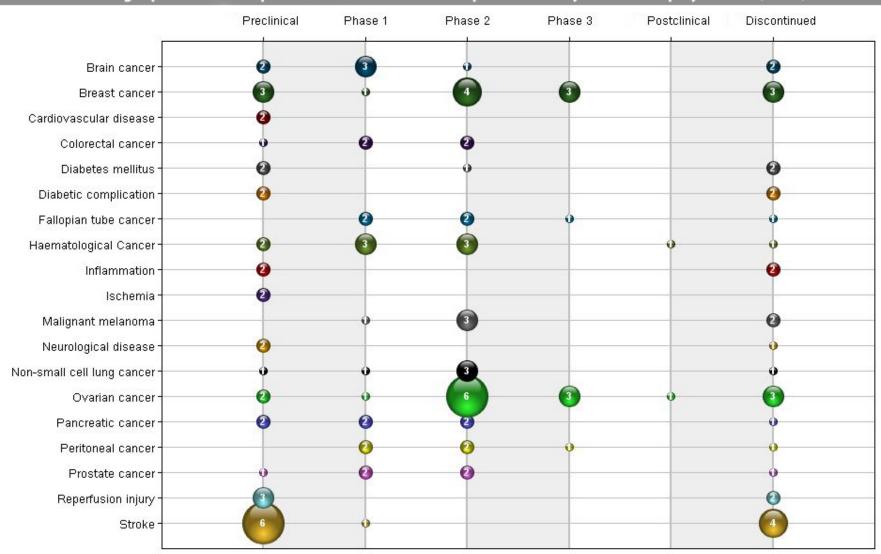
3	3	0 Biological Testing
43	43	0 Preclinical
7	7	1 Phase 1
8	8	2 Phase 2
9	9	3 Phase 3
3	3	5 Registration
1	1	6 Marketed
19	19	7 Discontinued
69	69	8 No Development Reported

Appetizer – Clean-up indications

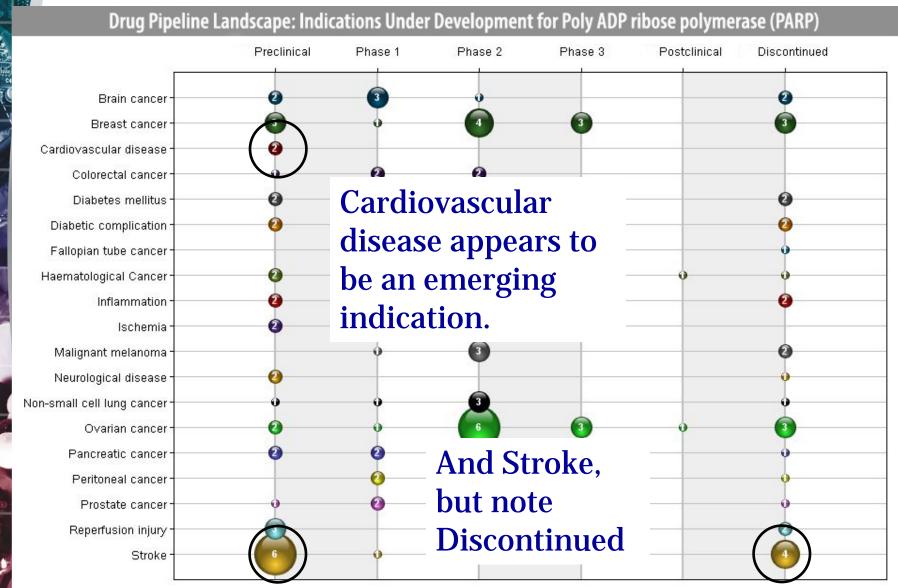


Appetizer - A sparkling pipeline landscape

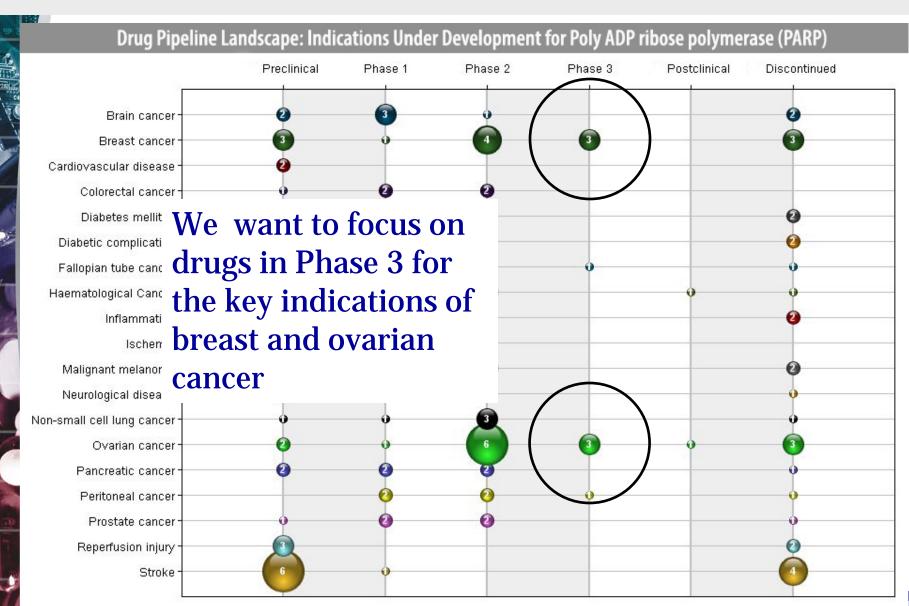
Drug Pipeline Landscape: Indications Under Development for Poly ADP ribose polymerase (PARP)



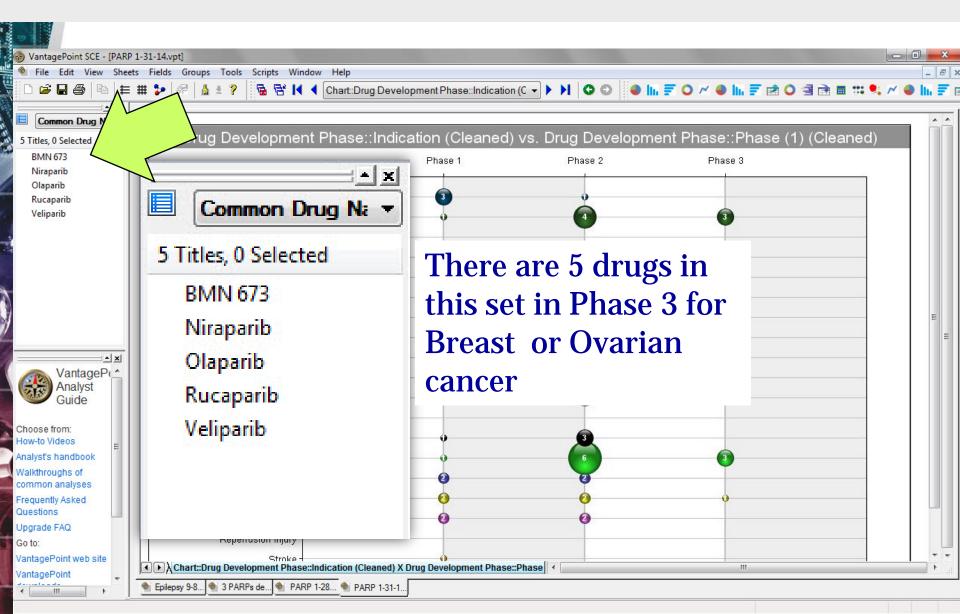
Appetizer: Identify drugs for further study



Appetizer: Identify drugs for further study



Appetizer: Identify drugs for further study



Continuing to explore our key ingredient



- Analysis of pipeline data shows which indications are being developed for a target and broadly what stage each is at.
- Clinical trial databases help you to see the details.

Entrée – Selection of Clinical Trial Timelines

The Challenge:

What trials are completed or planned for the key PARP drugs in development?

Background: A series of setbacks occurred in the early development of PARP inhibitors because the drugs were highly toxic when used in combination with chemotherapy, specifically in patients expressing the BCRA1 & BCRA2 genes. The toxicity caused myelosuppression. A retrospective analysis of genotyping of patients indicated the drug must be used in the right group. In 2014 the main determinant of trial success may be the Phase III trial design, where the drugs have the potential to help the BCRA population.

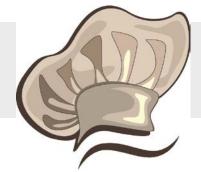
BizInt Smart Charts 2014

Entrée – Mise en Place/ Prep Work



- Searched for PARP inhibitors identified from the pipeline search (BMN-673, Niraparib, Rucaparib).
- Searched 3 clinical trials databases:
 - ClinicalTrials.gov 19 records
 - Citeline TrialTrove 25 records
 - Adis Clinical Trials Insight 21 records

Entrée – Design your Dish



Clinical trial databases help you evaluate the details of trials:

- Timing: has the trial just started or nearing completion?
- Status: is the trial still in planning, still enrolling, or active?
- Location: where is the trial being held and what is the targeted patient population?

Entrée – Recipe at a glance

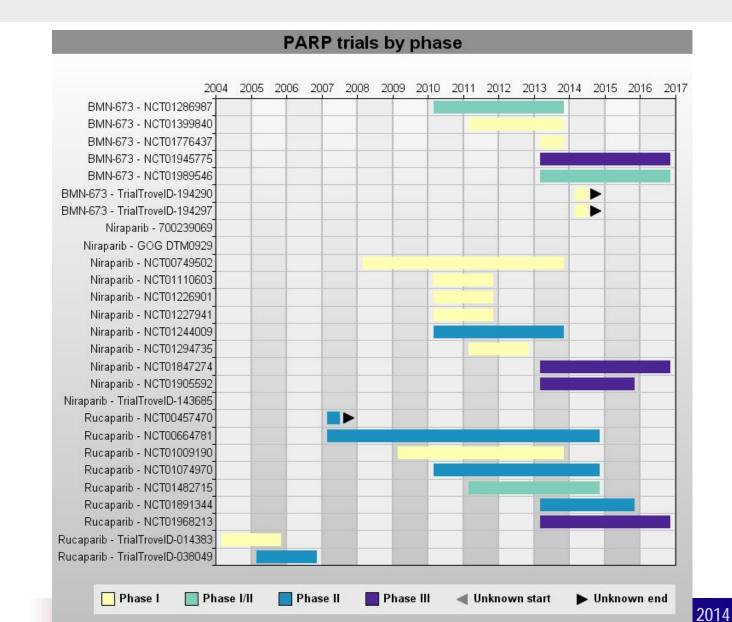
- Import results from each database and combine
- Send to Reference Rows to create a single row for each trial and export to VP-SCE.
- Using VantagePoint Smart Charts Edition:
 - Normalize phase and status fields
 - Normalize drug names
 - Create Timelines by phase and by status
 - Create map of trial locations



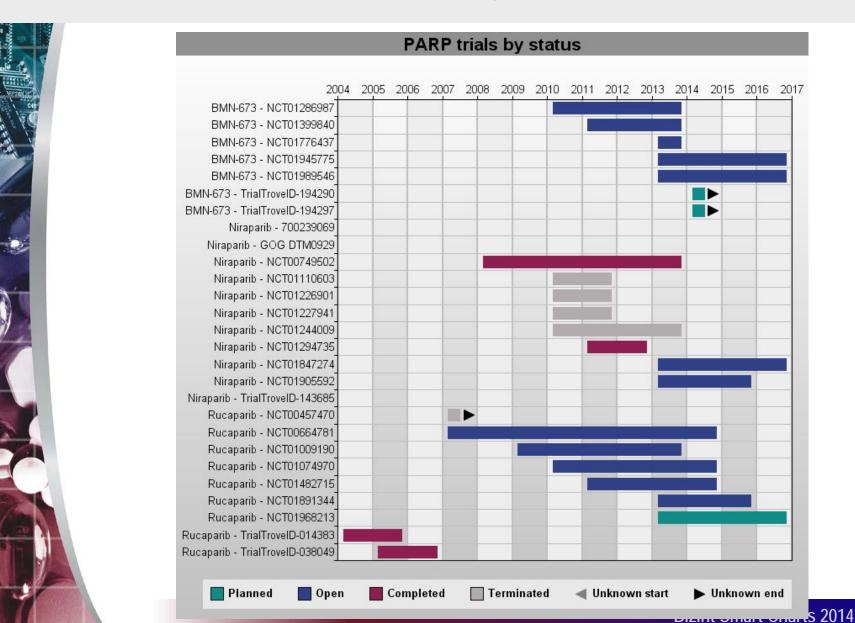
Entrée – Trial start and completion dates

					_	
	Trial Title	Comn	Database	Start Dat	e l	Completion Date
1 .1	A Parallel Arms Phase I Safety, Pharmacokinetic And Pharmacodynamic Study Of The Intravenous Poly (ADP-Ribose) Polymerase (PARP) Inhibitor PF-01367338 (AG-014699) In Combination With Several Chemotherapeutic Regimens In Adult	NCT0	Citeline TrialTrove	2009-01-01	*	Completion Date
1 .2	Patients With Advanced Solid Tumor A Parallel Arms Phase 1 Safety, Pharmacokinetic And Pharmacodynamic Study Of The Intravenous Poly (ADP-Ribose) Polymerase (PARP) Inhibitor PF-01367338 (AG-014699) In Combination With Several Chemotherapeutic Regimens In Adult Patients With Advanced Solid Tumor.	NCTO.				
1 .3	A Study Of Poly (ADP-Ribose) Polymerase Inhibitor PF-01367338 In Combination With Several Chemotherapeutic Regimens	NCT0	Adis Clinical Trials Database	01 Feb 2010 (actual)		01 Dec 2013 💉 (planned)
2 .1	A Cancer Research UK Phase II Proof of Principle Trial of the Activity of the PARP-1 Inhibitor, AG-014699, in Known Carriers of a BRCA 1 or BRCA 2 Mutation With Locally Advanced or Metastatic Breast or Advanced Ovarian Cancer	NCT0(
2 .2	A Cancer Research UK Phase II Proof of Principle Trial of the Activity of the Intravenous PARP-1 Inhibitor, AG-014699, in Known Carriers of a BRCA 1 or BRCA 2 Mutation With Locally Advanced or Metastatic Breast	NCT00	ClinicalTrials.Gov	February 2010)	November 2013
2 .3	or Advanced Ovarian Cancer. Rucaparib(CO-338;Formally Called AG-014699 or PF-0136738) in Treating Patients With Locally Advanced or Metastatic Breast Cancer or Advanced Ovarian Cancer	NCT00	S.I.III GATTI TIGO. GOV	. oblidary 2010		(Anticipated)

Entrée – Trial timeline by trial phase



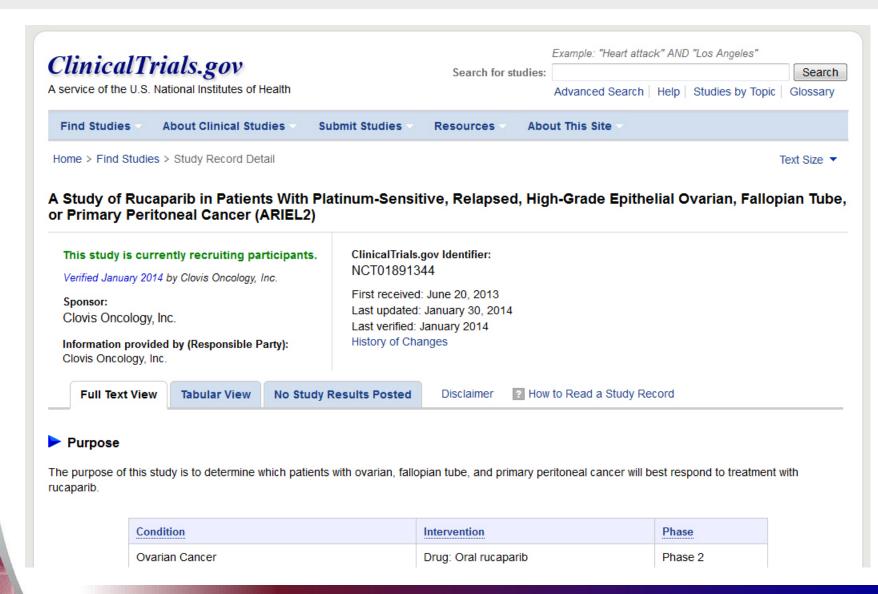
Entrée – Trial timeline by trial status



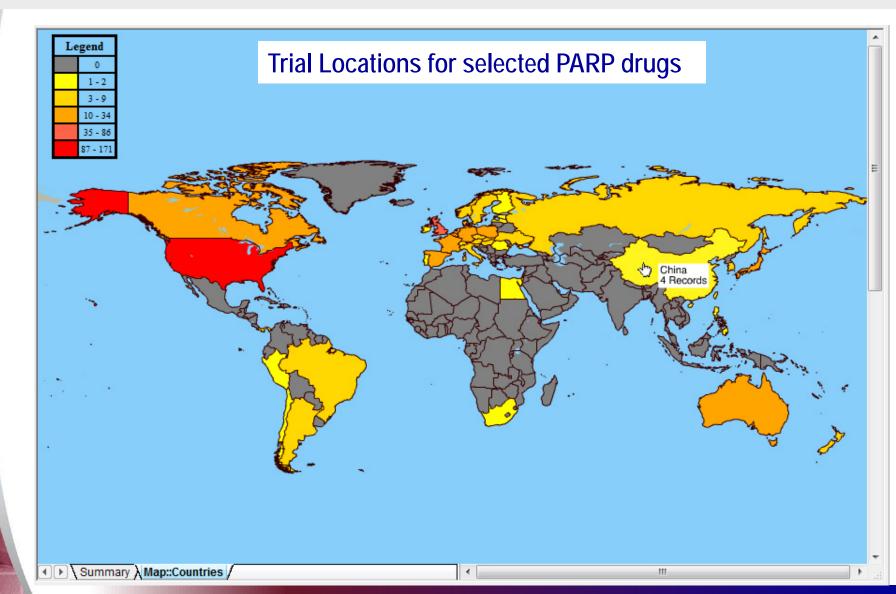
Entrée - Select trials for further review

	Trial Title	Common Trial ID	Database	Brief Summary	Phase	Countries	Overall Status	Enrollment
	18.1 NCT			18.2 ACT3	18.1 NCT	18.1 NCT	18.3 TROVE	18.2 ACT
19.	A Study of Rucaparib in Patients With Platinum- Sensitive, Relapsed, High-Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ARIEL2)		19.1 NCT tink 19.2 ACT3 tink 19.3 ACT3 tink 19.4 TROVE tink	This biomarker study is investigating the efficacy and tolerability of rucaparib phosphate [Clovis Oncology] in patients with platinumsensitive high-grade ovarian cancer, fallopian tube cancer, or primary peritoneal cancer. The primary endpoint is the best overall response assessed within 7 days of every odd numbered treatment course.	Phase 2	United States Australia Canada Spain United Kingdom	Open	540
	19.1 NCT			19.2 ACT3	19.1 NCT	19.1 NCT	19.4 TROVE	19.3 ACT
20.	A Study of Rucaparib as Switch Maintenance Following Platinum-Based Chemotherapy in Patients With Platinum-Sensitive, High-Grade Serous or Endometrioid Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer	NCT01968213	20.1 NCT link 20.2 TROVE link	Patients enrolled into this study will be stratified into 3 groups based on gene mutations identified in their tumor tissue. The purpose of this study is to identify which of these groups of patients will most likely benefit from treatment with rucaparib.	Phase 3	United States Australia Belgium Canada France Germany Israel Italy New Zealand Spain United Kingdom	Planned	540 (Anticipated)
	20.1 NCT			20.1 NCT	20.1 NCT	20.1 NCT	20.2 TROVE	20.1 NCT
21.	Rucaparib(CO-338;Formally Called AG-014699 or PF-0136738) in Treating Patients With Locally Advanced or Metastatic Breast Cancer or Advanced Ovarian Cancer	NCT00664781	21.1 NCT link 21.2 ACT3 link 21.3 TROVE link	This trial will investigate the efficacy and tolerability of rucaparib phosphate [AG014699, PF-1367338] in known carriers of a BRCA 1 or BRCA 2 mutation patients with locally advanced or metastatic breast or advanced ovarian cancer. [CONT.]	Phase 2	United Kingdom	Closed	114
	21.1 NCT			21.2 ACT3	21.1 NCT	21.1 NCT	21.3 TROVE	21.2 AC
22.	PARP Inhibition for Triple Negative Breast Cancer (ER./PR./HER2-)With BRCA1/2 Mutations	NCT01074970	22.1 NCT link 22.2 ACT3 link 22.3 TROVE link	This trial will investigate the efficacy and tolerability of cisplatin, with or without PF 1367338, as second-line therapy in patients with triple	Phase 2	United States	Closed	135 (Anticipated

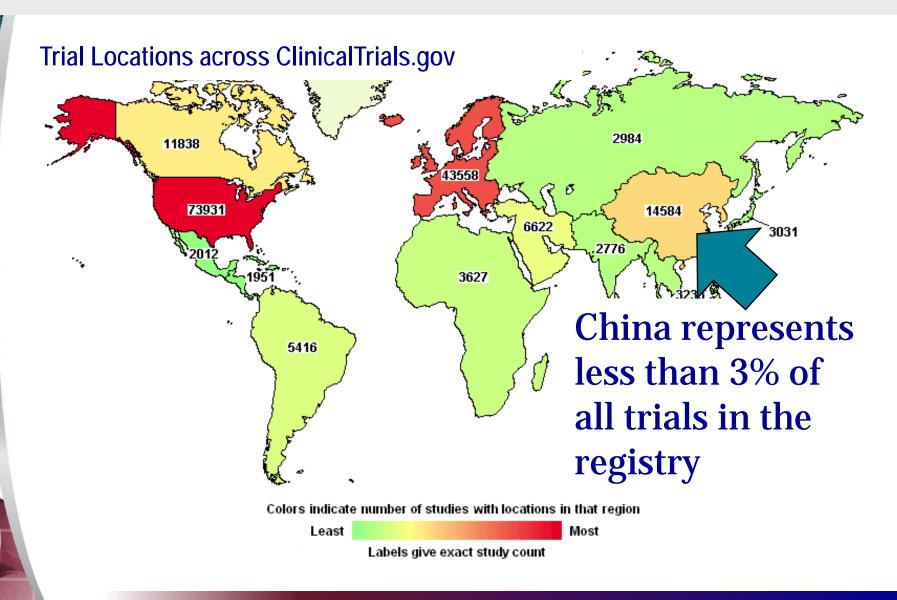
Entrée - Select trials for further review



Entrée Side – The World According to PARP



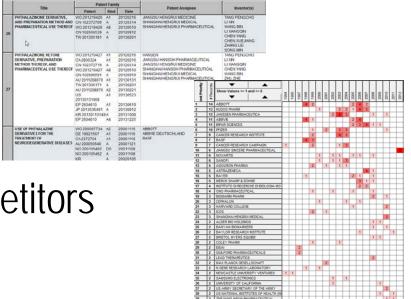
What about China?...



Dessert – Foray into Chinese Patent Data

The Challenge:

Who are the potential competitors or partners in China?



Background: Clinical trials can help us gauge the progress of competitors in a market. In order to identify other organizations which may become players within a market, we can look at patents filed in that market. Increased (or emergent) filing activity is a leading indicator for market entry.

Dessert – Choose your ingredients



- Many patent databases now provide coverage for Chinese publications, searchable in English.
- Terminology in machine translations may not be useful for keyword searching.
- Family based patent databases allow you to search equivalent documents in the original language (e.g. English)
- We use the Thomson Innovation with Derwent indexing for this example

Dessert – Mise en Place/ Prep Work

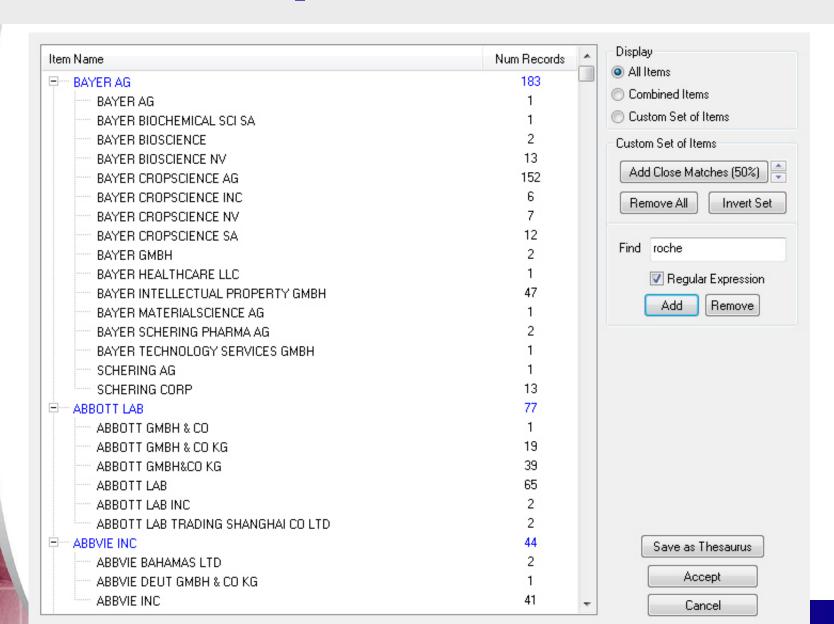


- Database: Thomson Innovation
- Query: 'PARP' or 'poly (adp-ribose) polymerase' in claims
- Limited to families containing 'CN' publication
- Total Result: 1203 publications representing 986 distinct families

Dessert – Recipe at a glance

- Create chart from search result
- Export earliest priority date, patent assignee to VP-SCE
- Normalize assignees using VP-SCE cleanup
- Extract priority year
- Create matrix graph to analyze competitors
- Review "interesting" records in BizInt Smart Charts for Patents

Dessert – Technique



Dessert - Identify the Potential Competitors

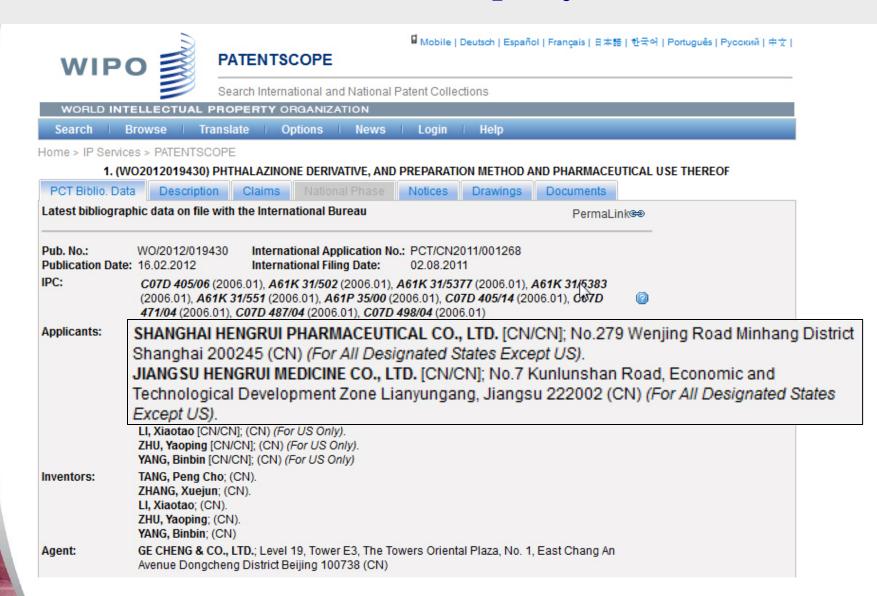
sie	100		Reset		Patent Assignee (Cleaned)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17		
	No				# Records	5	20	27	31	27	39	54	93	96	12	10	10	12	16	14	26	12		
STEE VEPT	000		Dates/F	# Recor	Y A	1994	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012		
of Sec.	16 C		1	167	BAYER AG	\Box		2	1				2	2	4	7	19	37	37	54	2			
in a			2	77	ABBOTT LAB	İ		5	4						3	9	5	9	21	18	3			
	7		3	44	ABBVIE INC			1							1	4	1	4	12	18	3			
			4	28	NOVARTIS AG					2			10	5	6	3	1		1					
			5	24	GENENTECH INC									5	9	2	1	3	2	2				
	6		6	23	BASF AG		1	5	5	1		3			2		2	1	3					
			7	21	KUDOS PHARM LTD	Ι.	١, ١		Ι.	2		I, I	6	3	1	6	3							
	32	6	JIAN	GSU	HENGRUI MEDICINE CO LTD																	6		
	33	6	JIAN	GSU	SIMCERE PHARM CO LTD							Т	Т	Т					Т	Т	Т		6	1
7	34	6	SHA	NGH	AI HENGRUI PHARM CO LTD							T	\top		\top				T	\top		6		1
V		^	12	16	PFIZER INC	Г			1		1	2	2	2		2	4	1		1	1	1	1	1
	4		13	14	SCHERING AG							1		3		6	3		1			\neg		
9			14	12	AGOURON PHARMA				3	2	2		2	2				1				\neg		
			15	11	CEPHALON INC		1			4				2		3			1					
			16	11	CHIRON CORP	ĺ							7	3	1									
			17	10	INOTEK PHARM CORP						2		4	2	1		1							
1			18	9	NEREUS PHARM INC							2	1	5	1									
			19	8	ASTRAZENECA AB											2	3	2		1				
			20	8	CYCLACEL LTD							1	1		1	1	2	2						
			21	8	IST RICERCHE BIOL MOLECOLARE ANGEL											4	4							
			22	8	XOMA TECHNOLOGY LTD								6		1		1							
			23	7	ACUCELA INC												5	2	11111					
d			24	7	AEGERA THERAPEUTICS INC							2	1		1	3								
	7		25	7	PFIZER PROD INC				1		1					1	4							
W.			26	7	XENCOR INC									4			2			1				
1		BA	27	6	AGENSYS INC									4	2									
			28	6	ALLERGAN INC														6				38	

Dessert - Select companies for further review

Key Chinese patent assignees for PARP (selected via co-occurence matrix)

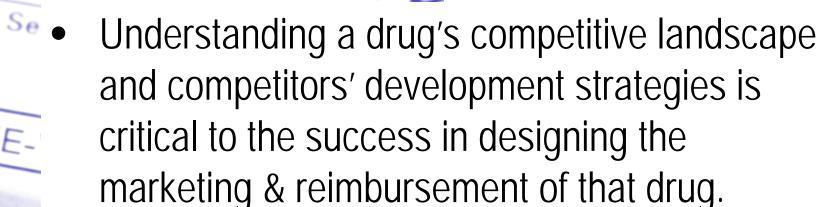
1. New phthalazinone compound useful in pharmaceutical composition for treating cancer, prostate cancer and rectal cancer 1.1 Innov	VS	Title	Patent Family			Patent Assignee	Inventor(s)	Database	CPC
1		Title	Patent	Kind	Date	Faterit Assignee	inventor(s)	Database	or c
Carcer e.g. breast cancer covarian cancer, prostate cancer and rectal cancer MO 2012019430 A 2012-02-16 TW 201307349 A 2013-02-16 TW 2013073181 A 2013-02-01 TW 201305181	1.	useful in pharmaceutical				SHANGHAI HENGRUI MEDICINE CO LTD	ZHU, Yao-ping		C07D040514
1.1 Innov		ovarian cancer, pancreatic cancer, prostate cancer and	CN 102762549	Α :	2012-10-31				
2. useful in pharmaceutical composition for treating cancer a.g. breast cancer, ovarian cancer, prostate cancer and rectal cancer 2.1 Innov 3. New phthalazinone ketone derivative useful in pharmaceutical composition for treating cancer e.g. breast cancer, prostate cancer, prostate cancer and rectal cancer WO 2012019427 AB 2012-09-10 SHANGHAI HENGRUI MEDICINE CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI MEDICINE CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI MEDICINE CO LTD SHANGHAI HENGRUI MEDICINE CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI HENGRUI MEDICINE CO LTD SHANGHAI HENGRUI PHARM CO LTD SHANGHAI PHAR					1.1 Innov	1.1 Innov	1.1 Innov		1.1 Innov
3. New phthalazinone ketone derivative useful in pharmaceutical composition for treating cancer, e.g. breast cancer, postate cancer and rectal cancer Mode	2.	useful in pharmaceutical composition for treating cancer e.g. breast cancer, ovarian cancer, pancreatic cancer, prostate cancer and	CN 102372706 WO 2012019426 CN 102666539	A A8 A	2012-03-14 2012-05-10 2012-09-12	SHANGHAI HENGRUI MEDICINE CO LTD	CHEN, Yang DENG, Bing-chu LI, Xiang-qin LI, Xin SONG, Min WANG, Bin		C07D040310 C07D047104 C07D048704 C07D0491048 C07D049504
derivative useful in pharmaceutical composition for treating cancer e.g. breast cancer, ovarian cancer, pancreatic cancer, prostate cancer and rectal cancer CN 102372716		2.1 Innov			2.1 Innov	2.1 Innov	2.1 Innov		2.1 Innov
3.1 Innov 3.1 Innov 3.1 Innov 3.1 Innov	3.	New phthalazinone ketone derivative useful in pharmaceutical composition for treating cancer e.g. breast cancer, ovarian cancer, pancreatic cancer, prostate	CN 102372716 WO 2012019427 CN 102686591 AU 2011288876 AU 2011288876 CA 2806324 TW 201305171 US 20130131068 EP 2604610 HK 1174030 JP 2013535491	A A8 A A1 A2 A1 A A1 A1 A0 A	2012-02-16 2012-03-14 2012-05-10 2012-09-19 2013-01-31 2013-02-21 2012-02-16 2013-02-01 2013-05-23 2013-06-19 2013-05-31 2013-09-12	JIANGSU HANSOH PHARM CO LTD JIANGSU HENGRUI MEDICINE CO LTD SHANGHAI HANSOH PHARM CO LTD SHANGHAI HENGRUI MEDICINE CO LTD	DENG, Bing-chu LI, Xiang-qin LI, Xin WANG, Bin		C07D048704 A61K00314188 A61K0031502
	i	3.1 Innov			3.1 Innov	3.1 Innov	3.1 Innov		3.1 Innov

Dessert – Drill down to company details



In Conclusion...





- BizInt Smart Charts and VantagePoint –
 Smart Charts Edition tools support the creation of visualizations & reports from drug pipeline, clinical trials and intellectual property databases
 - to facilitate those insights.

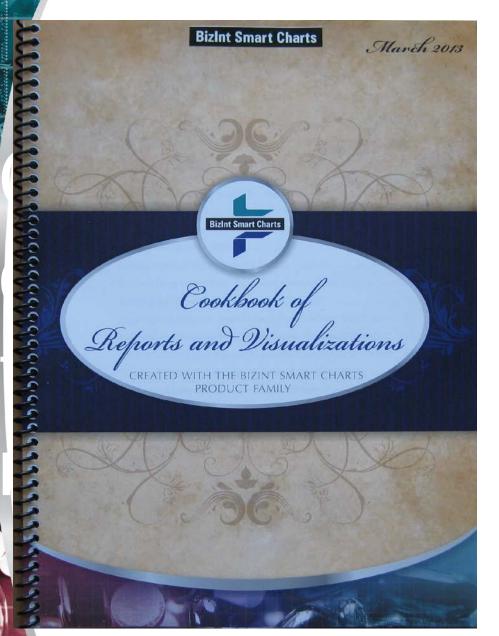
Thank you to our team of talented chefs!



Matt Eberle
Product Specialist
Formerly at Wyeth, Pfizer,
Sunovion



Barbara Gilmore
Application Consultant
Formerly Genentech, Kai





Come by our stand for more info and to see the Cookbook!

bizint.com/Cookbook