



Surfing the Pipeline: Drug Portfolio Analysis

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Surfing the Pipeline

Comparing pipeline databases

- First case study "Amgen" done in 2000
- Follow-on case studies in 2003: epilepsy, COX-2 inhibitors, TAP
- Updated epilepsy and TAP case studies in 2006
- HER-2 inhibitors – 2008 (in conjunction with Barbara Gilmore)

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Drug Pipeline Databases

The leading players

- **Pharmaprojects** – Informa (PJB)
- **R&D Focus** -- IMS Health
- **R&D Insight** – Wolters Kluwer Health (Adis)
- **IDdb/Thomson Pharma** – Thomson Reuters (Current Drugs)
- **Integrity** – Thomson Reuters (Prous Science)

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Drug Pipeline Databases

Compare the differences in...

- **Coverage** – number of compounds retrieved by each search.
- **Content** – information provided for each compound by each database.
- **Updating** – how compounds change in each database over time.

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Case study: HER2 inhibitors

Search strategies

- Searches done in April and June 2008
- PP: pharmacological activity = ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN)
- RDF: text contains "HER2"
- RDI: mechanism of action = HER2 inhibitors
- TPharma/IDdb: Action = Erbb2 tyrosine kinase receptor inhibitor
- Integrity: Action = HER2(erbB2) inhibitors

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Case study: HER2

Search results

■ <u>Records retrieved</u>	<u>April 08</u>	<u>June 08</u>
■ Pharmaprojects	77	77
■ R&D Focus	76	80
■ R&D Insight	35	39
■ Thomson Pharma	60	62
■ Prous Integrity	130	136

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Case study: HER2

Identifying unique compounds

	Drug	Synonyms	Common Drug Name	Database
126	MAb, HER2/neu, InNexus	DXL 702	DXL 702	IMS R&D Focus
127	DXL-702		DXL 702	PJB Pharmaprojects
128	DXL-702		DXL 702	Prous Integrity Compounds
129	Research programme: anti-HER2 monoclonal antibodies - InNexus Biotechnology	DXL 702 DXL702	DXL 702	Adis R&D Insight

“Generate Common Drug Names” tool automatically matches product names and synonyms

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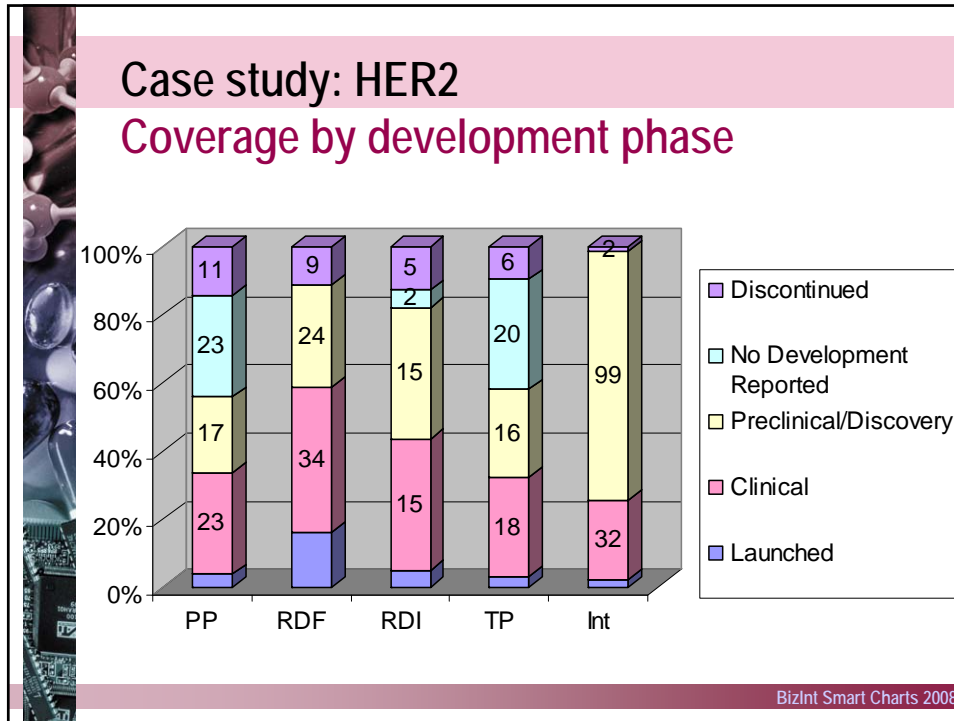
Case study: HER2 (June 08)

273 unique compounds in 394 records

Database	Percentage
PP	28%
RDF	29%
RDI	14%
TP	23%
INT	50%

% of unique compounds retrieved from each database

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Case study: HER2 inhibitors Search strategies

- Also searched the HER2 target tree (primary target = HER2 or HER2/NEU) in PP

PJB Pharmaprojects: pjb_her2_mech_jun08				
Product	Pharmacological Activity	Target Names	Search Strategy	
PX-104.1	ErbB-2 tyrosine kinase inhibitor (K-TYE2-AN) Immunostimulant (M-AG)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma	Mechanism	1
anti-ErbB-2 MAbs, Enzon	ErbB-2 tyros (K-TYE2-AN)			2
PKI-166	ErbB-2 tyros (K-TYE2-AN) ErbB-1 tyros (K-TYE1-AN)			2
				3

PJB Pharmaprojects: pjb_her2_jun08 target search				
Product	Pharmacological Activity	Target Names	Search Strategy	
2B-1	CD16 antagonist (CD-16-AN)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian) Fc fragment of IgG, low affinity IIIa, receptor (CD16) Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	Target	1
ABY-002	Not applicable (NA)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian)	Target	2
AE-37	ErbB-2 tyrosine kinase inhibitor (K-TYE2-AN) T helper cell stimulant (LYM-TH-AG)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian)	Target	3

Case study: HER2 inhibitors

Search strategies - Pharmaprojects

- Used the compare user comments feature to evaluate compounds retrieved by target vs. pharmacological activity/mechanism

Pharmacological Activity	Target Names	Search Strategy
Immunostimulant (IM-AG)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian)	Target
ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN) ErbB-1 tyrosine kinase inhibitor (KI-TYE1-AN) Endothelial growth factor receptor kinase inhibitor (KI-GFEN-AN)	v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian) epidermal growth factor receptor (erythroblastic leukaemia viral (v-erb-b)	Mechanism /Also/ Target

Case study: HER2 inhibitors

Search strategies - Pharmaprojects

Mechanism, 31

Target, 32

Mechanism /Also/ Target, 46

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Case study: HER2 inhibitors

Search strategies - Pharmaprojects

PJB Pharmaprojects: PP - HER2 searched by mech and target

	Product	Pharmacological Activity	Target Names	Search Strategy
83	INSM-18	Insulin like growth factor 1 antagonist (GF-IN-1-AN) ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN) IGF-1 receptor tyrosine kinase inhibitor (KI-GFIN1-AN)	insulin-like growth factor 1 receptor v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian)	Mechanism
84	anticancer MAbs, Xencor-2	CD20 antagonist (CD-20-AN) ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN)	membrane-spanning 4-domains, subfamily A, member 1 v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian)	Mechanism
85	T-3100	Oncogene inhibitor (ONCOG-AN) ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN) Myc inhibitor (MYC-AN)	v-myc myelocytomatosis viral oncogene homologue (avian) v-erb-b2 erythroblastic leukaemia viral oncogene homologue 3 (avian)	Mechanism

Why were these compounds not retrieved by the target search?

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Case study: HER-2

RDI – “missing records”

- Strategy: mechanism of action = HER2 inhibitors
- AE-37: mech = immunostimulants
- BMS 690514: mech = Epidermal growth factor receptor antagonists, Protein-tyrosine kinase receptor antagonists
- CAB 051: mech = Epidermal growth factor receptor antagonists
- E 75: mech = T cell stimulants
- HER-2 Protein AutoVac: mech = Epidermal growth factor inhibitors, Immunostimulants
- JNJ-26483327: mech = Epidermal growth factor receptor antagonists, Protein tyrosine kinase inhibitors

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Case study: HER-2

Conclusions on coverage variation

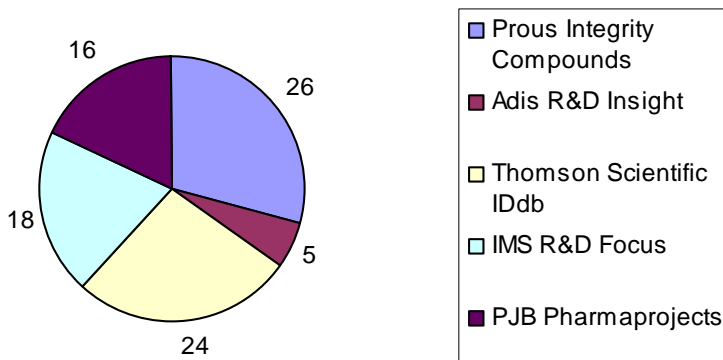
- Different compounds are retrieved from each database because of differences in **indexing**.
- A search of any single database will retrieve only 20-40% of the unique compounds.
- Searches will need to be revised to identify "missing" records, especially for topics like HER-2.

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Case study: HER2

Updated and Added Records

Number of Updated Records (Apr08 - Jun 08)



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Case study: HER-2 Coverage Variation – “Reference Rows”

Drug	Row Status	Source	Status	Action	Structure	CAS Number
3 ▼	3.1 Updated	3.1 PP 42195	Phase III Clinical Trial	ErbB-1 tyrosine kinase inhibitor (KI-TYE1-AN) ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN)		438081-18-2 438081-17-1 (enantiomer)
	3.2 Updated	3.2 INT 323397				
	3.3 Updated	3.3 IDDB 54449				
	3.4 Unchanged	3.4 RDI 800023647				
	3.5 Unchanged	3.5 RDF 2027163				
3.1	Updated	42195	Phase II/III	ErbB-1 tyrosine kinase inhibitor (KI-TYE1-AN) ErbB-2 tyrosine kinase inhibitor (KI-TYE2-AN)		438081-18-2 438081-17-1

Cell Selection Rules

Choose from the rules below to determine how the Reference Row cell for this column will be selected.

Most recently updated record

Highest Phase

Most content in cell

Database preference

Adis R&D Insight
IMS R&D Focus
Thomson Pharma
Prous Integrity
Informa Pharmaprojects

Records

Select on Publisher Website

Publisher Images

Column Properties...

Row Properties...

Add Row

Hide Row Ctrl+H

Highlight cells Ctrl+L

Highlight rows Ctrl+Shift+L

Cut Ctrl+X

Copy Ctrl+C

Paste Ctrl+V

Font...

Quick format

Reference Row Rule


Select this cell

Help

About...

Case study: TAP Coverage Variation – “Reference Rows”


Drug	Common Drug Name	Row Status	Source	Synonyms	Company	Status	Action	Indication
1 ▶	A 198401		1.1 RDI 13007		Abbott Laboratories	No development reported	Gonadotropin releasing hormone antagonists	Female infertility
2 ▶	A 84861	2.1 Unchanged 2.2 Updated 2.3 Added	2.1 PP 27335 2.2 RDI 10049 2.3 Int 281737	ABT-861	Abbott (USA)	Preclinical	LHRH antagonist (LHRH-AN)	Female infertility Male infertility Prostate cancer
3 ▶	AGM-1470	3.1 Unchanged 3.2 Unchanged 3.3 Updated 3.4 Unchanged 3.5 Updated	3.1 Int 161076 3.2 RDI 1587 3.3 RDF 3.4 PP 16400 3.5 ID DR2441	fumagilil analog AGM-1470 NSC-642042 AG-1470 AGM-1683	Harvard University (USA) Takeda (Japan)	Discontinued(I)	Angiogenesis inhibitor (ANGG-AN) Endothelial growth factor antagonist (GF-EN-AN) Fibroblast growth factor antagonist (GF-FB-AN)	Glioma Sarcoma Pancreas tumor Prostate tumor Uterine cervix tumor Microsporidial infection Breast tumor Carcinoma Cancer Lung tumor Brain tumor Kaposi sarcoma Renal tumor
4 ▶	Asoprisnil	Reference Row	3.1 RDF 3.2 ID DR34739 3.3 INT 223488 3.4 RDF 2010181	asoprisnil J 887	Jenapharm (Germany)	Phase 3 Clinical	Selective Progesterone Receptor Modulators (SPRM)	endometriosis hormone deficiency fibroids



Surfing the Pipeline

Keep in mind...

- Drug pipeline records are not abstracted from a reference document (as with patents)
- Each record is an **editorial view** of the compound based on a range of sources.
- Each publisher has a unique background and focus.
- 10-20 editors at each publisher are maintaining several thousand active compounds.



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