Office of Oncology Drug Products: Drug Product Reviews

Approvals from July, 2005 (inception of Office) to December, 2007

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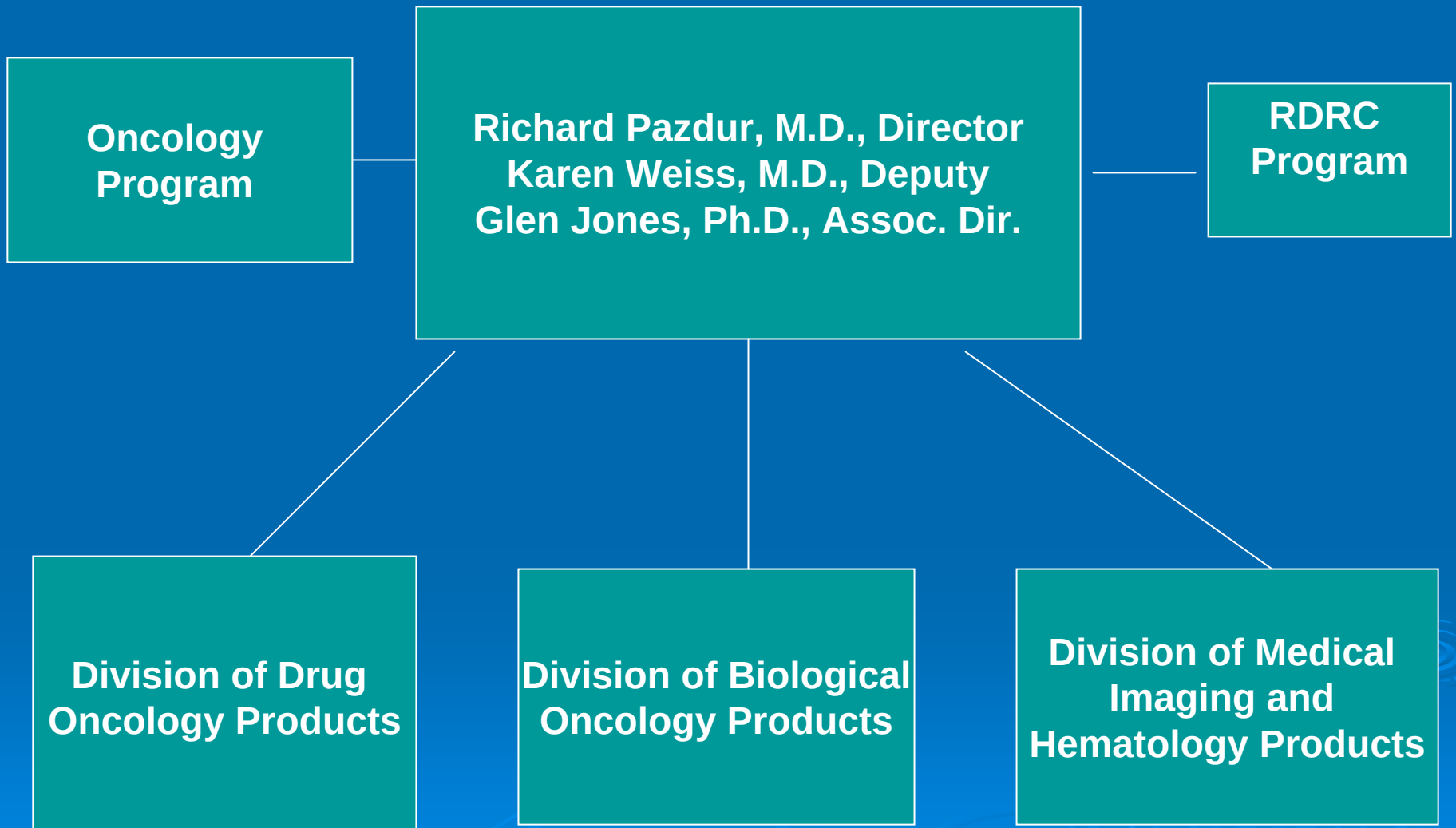
Thanks to All Members of OODP

Outline of Slides

- Products Reviewed during July 2005 – December 2007
- Products Approved
- Products Not Approved
- Applications Withdrawn
- Summary

Office of Oncology Drug Products



Indications Reviewed 7/05 – 12/07

- Includes drugs/biologics reviewed in Office of Oncology Drug Products
- Product categories: biological anticancer products reviewed by DBOP, anticancer drugs reviewed by DDOP, and hematology products reviewed by DMIHP
- Does NOT include indications reviewed by CBER or CDRH or radiopharmaceutical products reviewed by DMIHP

Indications Approved during July, 2005 to December 2007

- During this period of time, 53 new indications (18 New Molecular Entities) were approved
- During this same time period, only 5 indications (5 New Molecular Entities) were not approved
- During this same time period, only two applications were withdrawn by the Sponsor
- 7/05 – 12/05: 8 indications approved
- 1/06 – 12/06: 28 indications approved
- 1/07 – 12/07: 17 indications approved

Products Approved

- Of the 53 new indications—
- 39 priority and 14 standard reviews
- 18 New Molecular Entities (NMEs), 35 supplemental applications (sNDAs or sBLAs)

Types of Approvals

- 38 Regular Approval indications (demonstration of clinical benefit)
- 10 Accelerated approval indications
- 5 previous accelerated approvals converted to regular approvals (completion of confirmatory trials with new indication)

Endpoints Used in Approved Indications

- *Overall survival*: 10 indications
- Progression-free survival/Overall survival: 3 indications
- *Disease-free survival*: 5 indications
- *Progression-free survival or time-to-progression*: 12 indications
- *Response rates (includes CR, ORR, MCyR, MHR):* 16 indications
- *Other endpoints: 7 indications; Examples of novel endpoints*: reduction in hepatic iron, depletion of asparagine

Endpoints Used in Approved Indications

- *Progression-free survival or time-to-progression*: 12 indications –
  - 11/12 received full approval
  - FA Indications: Metastatic Renal cell carcinoma (2), Multiple myeloma (2), GIST, Metastatic Ovarian cancer, B-cell NHL (2), metastatic Breast cancer (2). B-cell Chronic lymphocytic leukemia
  - AA indication: Metastatic colorectal cancer

Endpoints Used in Approved Indications

- *Response rates (includes CR, ORR, MCyR, MHR):* 16 indications –
  - 3/16 full approvals
  - Full approval indications: MDS, Ph+ ALL, Neoplastic meningitis
- *Other endpoints: 7 indications –*
  - 3/7 full approvals
  - Full approval indications: ALL, Extravasation from IV anthracycline, Anemia associated with chronic renal failure

Trial Designs

- Randomized studies: 36
- Range of Sample sizes: 118 (ALL-pagaspargase) – 19,747 (Prevention of invasive breast cancer – raloxifene)

- Single arm Studies: 19
- Range of Sample sizes: 18 (Dermatofibrosarcoma protuberans (DFSP) – imatinib mesylate) – 445 (CML and ALL – dasatinib)

Examples of Approvals for “Rare” Diseases

- *Imatinib mesylate*: Dermatofibrosarcoma protuberans; Aggressive systemic mastocytosis;Hypereosinophilic syndrome/chronic eosinophilic leukemia; Relapsed/refractory pediatric PH+ ALL
- *Vorinostat*: Cutaneous T-cell lymphoma
- *Bortezomib*: Mantle cell lymphoma
- *Eculizamab*: Paroxysmal Nocturnal Hemoglobinuria

Noteworthy Approvals

- Advanced Renal Cell Carcinoma: sorafenib, sunitinib,Torisel (multiple agents for single disease)
- Hepatocellular Carcinoma: sorafenib (first drug to demonstrate a survival advantage for hepatocellular carcinoma)
- Mantle cell lymphoma: bortezomib
- Multiple myeloma—thalidomide, lenalidomide, doxil (multiple agents for disease)
- Supportive care—Exjade (iron overload), dalteparin (DVT in cancer patients), dexrazoxane (treatment of drug extravasation)
- Pediatric populations—nelarabine, deferasirox, imatinib, pegaspargase

Products Not Approved

- Genasense for CLL
- Atrasentan for HRPC
- Oral beclomethasone dipropionate for GVHD
- Xcytrin for brain metastasis from NSCLC
- Mifameratide for adjuvant osteosarcoma
- Four of the above did not meet primary endpoint of pivotal registration trial

Applications Withdrawn by Sponsor prior to FDA action

- Satraplatin
- Glucarpidase

Summary: July 2005 to December, 2007

- 53 new indications (18 NMEs and 35 supplemental BLAs/NDAs)
- During same period, only 5 indications (5 NMEs) were not approved; 4 of these failed primary endpoints of pivotal trial
- During same period, only 2 indications (2NMEs) were withdrawn by sponsor prior to regulatory action.

Summary: July 2005 to December, 2007

- Approvals included regular approvals (38), accelerated approvals (10), and conversions of prior accelerated approvals to regular approvals with new indications (5)
- Variety of endpoints used: overall survival (10), DFS (5) , PFS or TTP (12), response rate (16)
- Novel surrogate endpoints used based on understanding of drug's mechanism—depletion of enzyme, reduction of hepatic iron concentrations

Summary: July 2005 to December, 2007

- Pediatric indications/populations studied: Exjade, pegaspargase, nelarabine, imatinib supplements
- Supportive care products: Exjade (iron overload, dalteparin (DVT in cancer patients), dexrazoxane (anthracycline extravasation), cytarabine (neoplastic meningitis)

Web References

- Genesense: http://www.genta.com/index.php?option=com_content&task=view&id=60&Itemid=&CID=36&SHID=&COID=
- OrBec: http://www.dorbiopharma.com/news.htm
- Xcytrin: http://ir.pharmacyclics.com/releasedetail.cfm?ReleaseID=283134
- Mifameratide: http://www.medicalnewstoday.com/articles/80732.php
- Satraplatin: http://www.gpc-biotech.com/en/news_media/press_releases/2007/07-30-2007.html
- Glucarpidase: http://www.nelm.nhs.uk/Record%20Viewing/viewRecord.aspx?id=581187