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 Approved
- Products Not Approved
- Applications Withdrawn
- Summary
Office of Oncology Drug Products

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Oncology Program

Division of Drug Oncology Products

Division of Biological Oncology Products

Division of Medical Imaging and Hematology Products

RDRC Program
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- During this same time period, only two applications were withdrawn by the Sponsor.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

- \textit{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, pegasparagase
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, pegasparagase, nelarabine, imatinib supplements

- Supportive care products: Exjade (iron overload, dalteparin (DVT in cancer patients), dexrazoxane (anthracycline extravasation), cytarabine (neoplastic meningitis)
Web References

- **OrBec:** [http://www.dorbiopharma.com/news.htm](http://www.dorbiopharma.com/news.htm)
- **Mifamertide:** [http://www.medicalnewstoday.com/articles/80732.php](http://www.medicalnewstoday.com/articles/80732.php)
- **Glucarpidase:** [http://www.nelm.nhs.uk/Record%20Viewing/viewRecord.aspx?id=581187](http://www.nelm.nhs.uk/Record%20Viewing/viewRecord.aspx?id=581187)