RTOR – The Race is on

Dipti Patil & Hemangini Gurlani

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Background

- Regulatory agency and pharma industry are continuously making efforts to reduce drug development process to get fast access to new medicine
- Regulatory efforts
  - Priority review 1992
  - Accelerated approval 1992
  - Fast track filing 1997
  - Breakthrough therapy (BTD) 2012
- Approval of drug with 452 patients study within two weeks of sNDA filling – can we think of it?
- To accelerate drug development FDA OCE announced the **pilot program** in June 2018

Background continued..

- Real Time Oncology Review – ***RTOR***
  - Process for earlier review of data prior to full application submission
- Significant step in clinical research
  - Efficient review process
  - To reduce time for drug approval without compromising safety and effectiveness of treatment
- Acceptance into the RTOR does not guarantee or influence approvability of the supplement, which is subject to the usual benefit-risk evaluation by FDA scientists
- A win-win situation across the board for industry, FDA, health care providers and patients

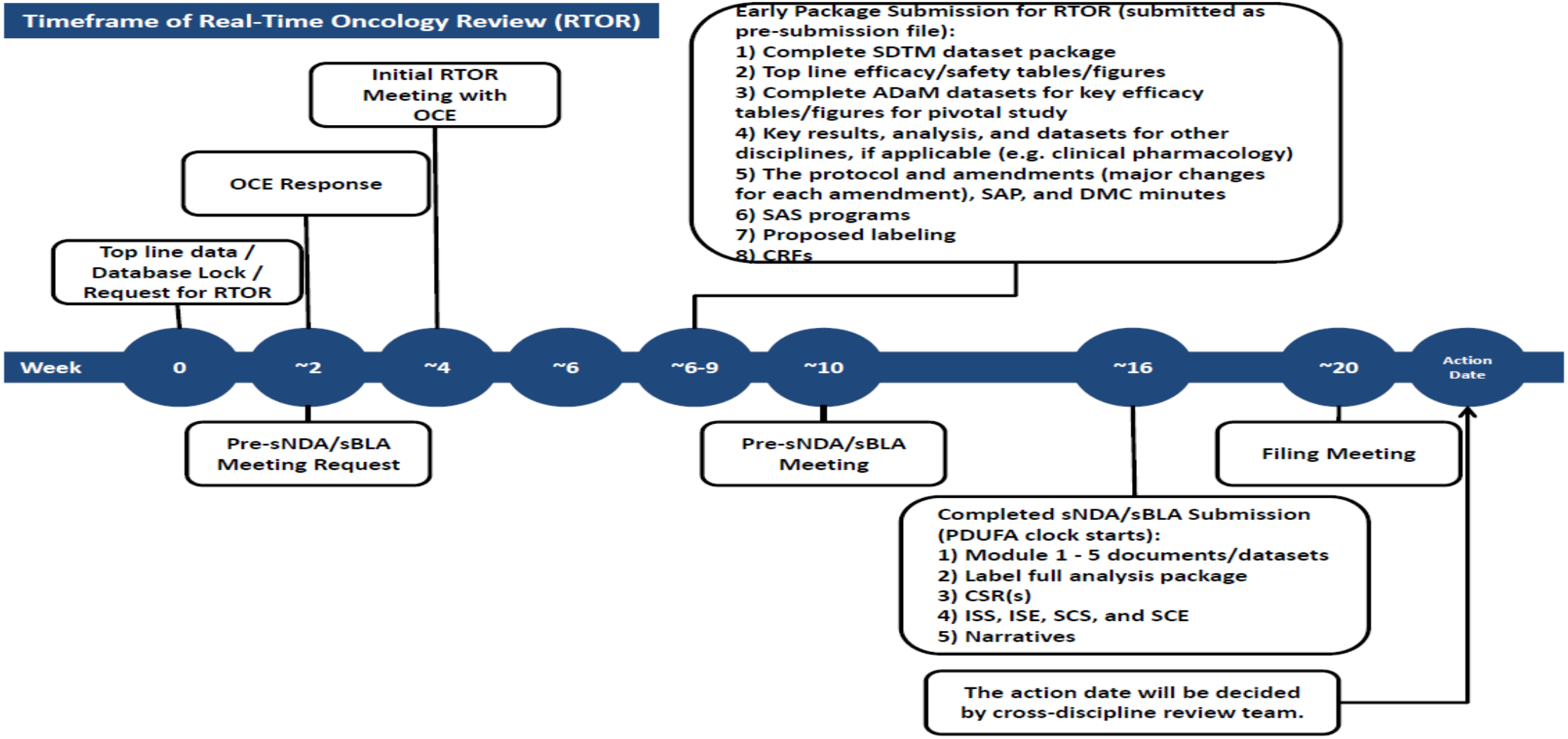
Eligibility criteria

Flexibility may be exercised at the discretion of the review division

- ✓ Drugs participating in an expedited program
- ✓ Straight-forward study designs
- ✓ Endpoints that can be easily interpreted

- × Studies conducted exclusively outside the United States
- × Supplements with CMC formulation changes
- × Submissions with companion diagnostics

Process



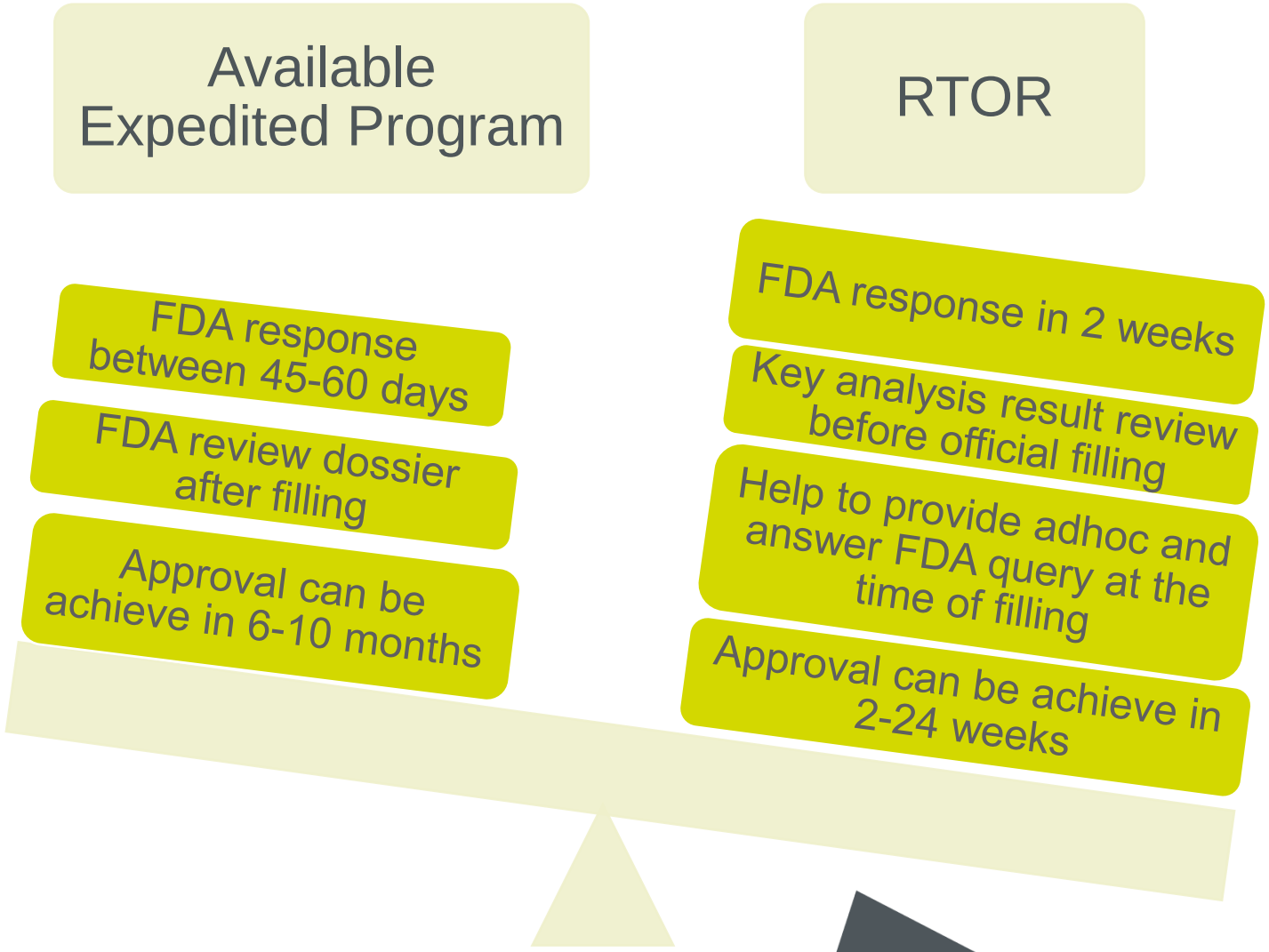
https://www.fda.gov/about-fda/oncology-center-excellence/real-time-oncology-review-pilot-program

Challenges

- Resourcing
  - FDA as well as sponsor side

- Streamline and improve efficiency on the sponsor’s end
  - Task which is usually completed in months, needs to be done in weeks
  - CDISC compliance - Legacy study submission
  - Handle any potential change on the dataset delivered earlier as part of RTOR

Added bonus – program comparison



Success stories

- KISQALI® (ribociclib)[1] - Novartis drug the 1st product approved under pilot receiving an expanded breast cancer indication, just 3 weeks after the sNDA filed
- KEYTRUDA® (pembrolizumab)[2] - Merck (five months)
- KYPROLIS® (carfilzomib)[3] - Amgen (one month)
- ADCETRIS® (brentuximab vedotin)[4] - Seattle Genetics (two weeks)
- TIBSOVO® (ivosidenib)[5] - Agios Pharmaceuticals
- KADCYLA® (ado-trastuzumab emtansine)[6] - Roche
- VENCLEXTA® (venetoclax)[7] – AbbVie & Roche
- DARZALEX® (daratumumab)[8] - Janssen Pharmaceutical Companies

[1] https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-drug-through-new-oncology-review-pilot-enables-greater-development

[2] https://investors.merck.com/news/press-release-details/2019/FDA-Approves-KEYTRUDA-pembrolizumab-plus-LENVIMA-lenvatinib-Combination-Treatment-for-Patients-with-Certain-Types-of-Endometrial-Carcinoma/default.aspx

[3] https://www.amgen.com/media/news-releases/2018/10/fda-approves-kyprolis-carfilzomib-onceweekly-70-mgm2-in-combination-with-dexamethasone-kd70-for-patients-with-relapsed-or-refractory-multiple-myeloma/

[4] https://www.fda.gov/news-events/press-announcements/fda-approves-first-line-treatment-peripheral-t-cell-lymphoma-under-new-review-pilot

[5] http://investor.agios.com/news-releases/news-release-details/agios-announces-fda-acceptance-supplemental-new-drug-application

[6] https://www.gene.com/media/press-releases/14785/2019-05-03/fda-approves-genentechs-kadcyla-for-adju [7] https://www.roche.com/media/release 019-05-16b.htm

[8] https://www.jnj.com/janssen-submits-application-to-u-s-fda-seeking-approval-of-darzalex-daratumumab-combination-therapy-for-patients-with-newly myeloma-who-are-transplant-ineligible

Pilot expansion

- Complex supplemental applications  simple breakthrough-designated new molecular entity (NME) NDAs/BLAs  complex NDAs/BLAs
- Identification of potential barriers
- Recommend policy to address those barriers
- Consideration
  - Align CDRH processes
  - Align manufacturing processes and inspections
  - Align clinical site inspection processes
- First **NDA** approved within 6 months
  - Piqray (alpelisib) – Novartis

https://www.focr.org/sites/default/files/pdf/2018_Friends_Scientific_Book_0.pdf
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-alpelisib-metastatic-breast-cancer

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https://www.focr.org/sites/default/files/ROTR%20White%20Paper%201.pdf

Questions & Answers

Thank you