Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Practical Barriers in Cancer Immunotherapy Treatment

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AAEM American Academy of Emergency Medicine — Champion of the Emergency Physician

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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Disclosures

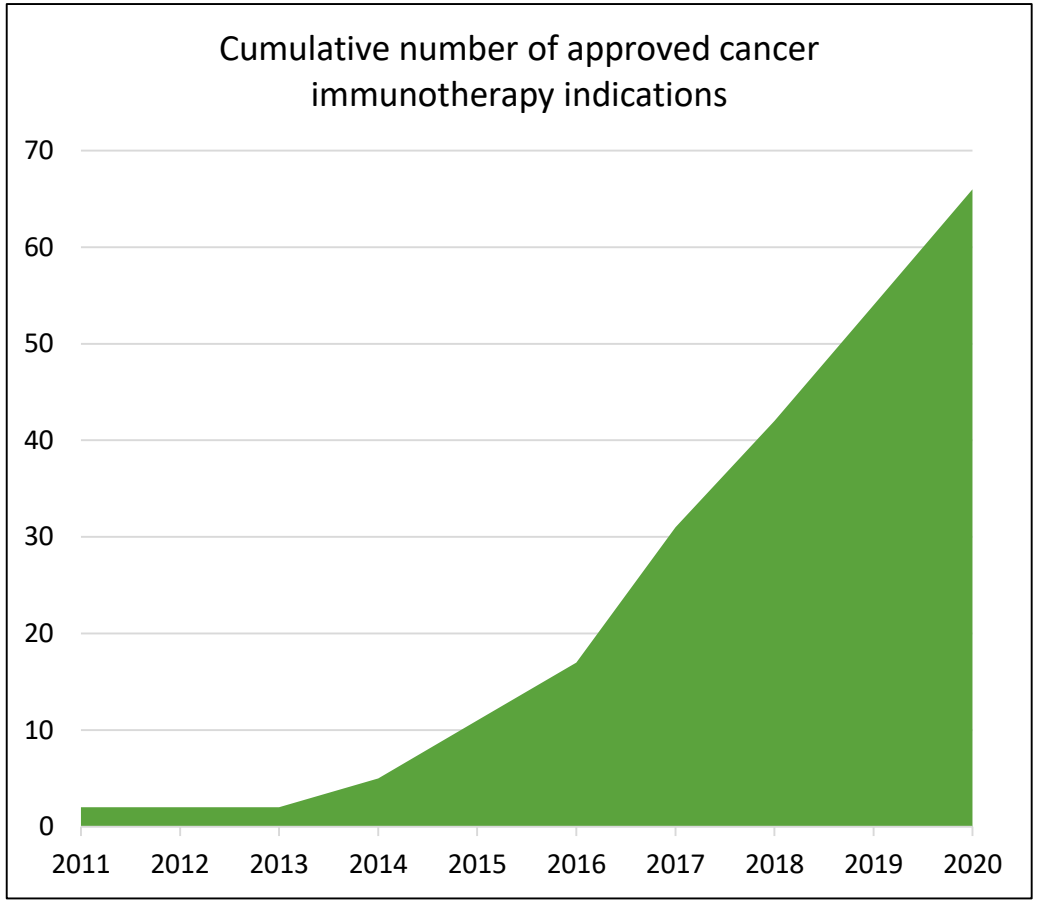
- No relevant financial relationships to disclose
- I will be discussing non-FDA approved indications during my presentation.

Outline

- Practical aspects of immunotherapy
- Financial considerations
- Medicare reimbursement
- Commercial payers
- New considerations for cancer immunotherapy

IO Pipeline and Research

- Current products on the market are the "tip of the iceberg" when looking at manufacturers' Immuno-Oncology (I-O) pipelines
- During the next few years, we can expect a new IO product or indication every few months
- Many new combinations and regimens with approved agents as well
- Important to help patients understand that they are receiving immunotherapy



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Strategies for New Information

- Immuno-Oncology Champion
  - Identify an "Immuno-Oncology Champion" from among your providers to be the "I-O point person" responsible for all product questions and staff education (can be physician, advanced practitioner or pharmacist)
- Education group
  - Identify a core group within your practice to manage patient education, including the review of existing patient materials and/or the development of new materials specific to I-O agents and management of their adverse effects
- Staff education
  - Proactively update staff on new information and consider use of manufacturer-provided resources including on-site training/education (or attend programs like this!)
- Identify specialty providers within your institution with expertise in immunotherapy toxicities
  - Developing a network of providers to prepare for all potential side effects from immunotherapy treatments (cardiac, pulmonary, gastrointestinal, neurology, etc)

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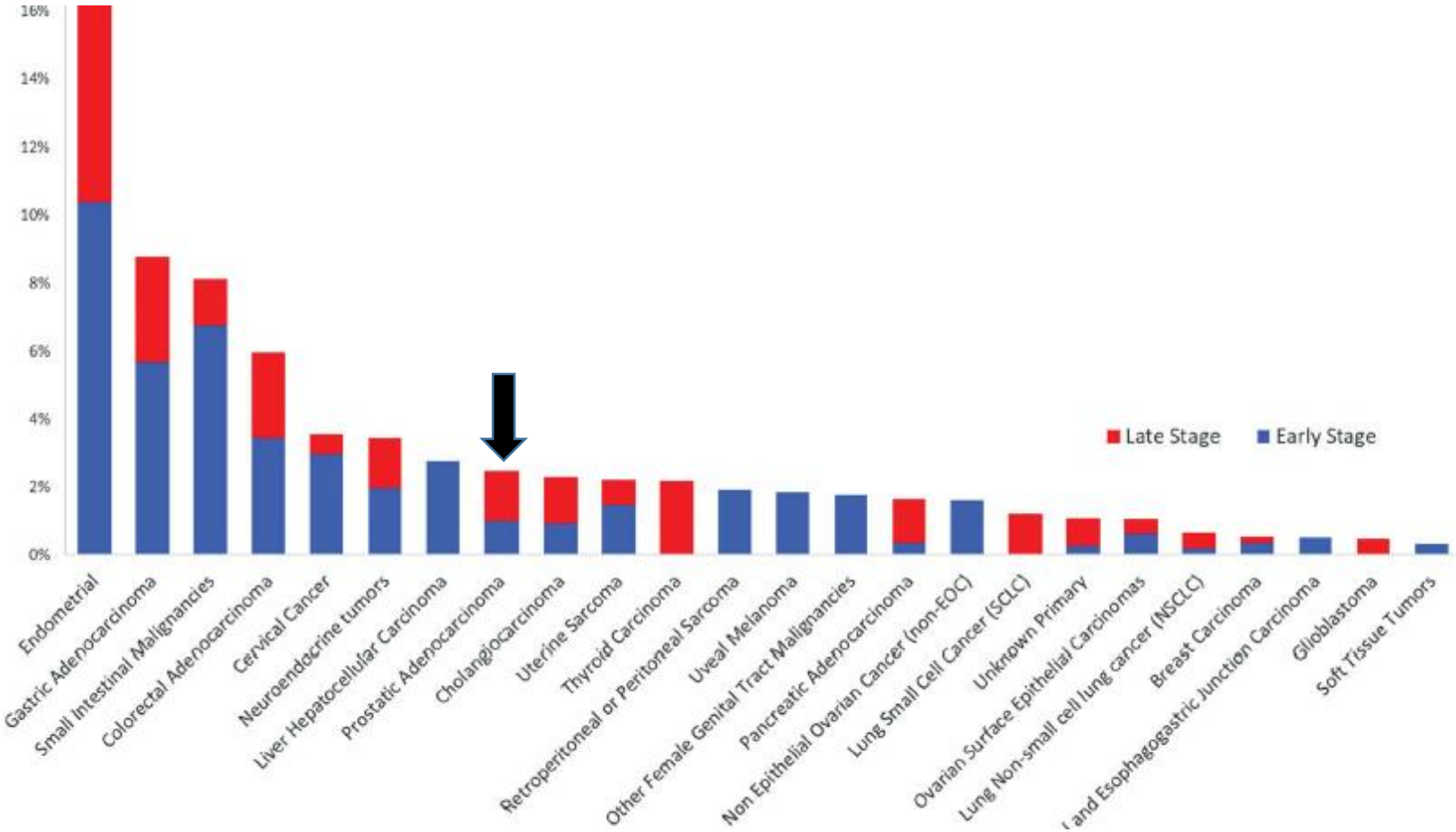
Case study: Mr. A

- Mr. A was diagnosed with metastatic castration resistant prostate cancer. His cancer had become resistant to androgen deprivation therapy and next generation androgen targeting agents. I sent tissue from his original surgery in 2019 for sequencing. His tumor had mismatch repair deficiency!

MMRD in Various Cancers



Le *et al.*, *Science* 357, 409–413 (2017) 28 July 2017

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Develop Approval Process

- High dollar medication approval process
  - Full benefits investigation, utilize pharma services if offered and allowed per hospital/institution policy
  - Prioritize staff resources to enroll every viable patient into a support program, regardless of on or off-label
- Robust off-label policy and procedure
  - All off-label requests require predetermination
  - Patients are made aware of risks and benefits, including financial risk
  - Patients are required to sign an advance beneficiary notice (ABN) or notice of non-coverage (NONC)
  - Peer review process for appeal if needed

Denials – Common Reasons

- Lack of pre-certification or authorization
- Does not meet medical necessity
- Considered experimental and investigational
- Requires additional information
- Non-covered service/medication on the plan benefit
- Out of network provider
- Timely filing of claims
- Multiple diagnoses coding for disease states and metastases - payer does not apply correct codes to medications
- Error in number of units billed to payer
- Insurance duplicity or delay
- Precertified at an alternate facility previously
- **Lack of education of insurance company employees**

General Rules for Denials

- Discover the root cause of the denial
  - Review payer-specific policy, local coverage determinations, national coverage determinations (LCDs & NCDs)
  - Determine if pre-certification or prior authorization was completed
  - Review documentation
    - Reimbursement is linked to the quality of the bill
    - Coders obtain information from medical record but sometimes required information is missing
- Look for denial trends with payers
  - Drugs, diagnosis, charge threshold
- Determine if dose billed for exceeds total units allowable

Handling Denials

- Work with Finance to develop a method for routing denials to appropriate personnel
  - Leverage IT to create work queue and notification process
- Consider appropriateness of resources
  - Workload (average number of denials/appeals)
  - Strict appeal timelines of many payers
- Consider training/experience of personnel
  - Ideally a nurse, pharmacist, or pharmacy technician with oncology experience
  - Ability to learn and understand financial systems and processes
  - Ability to navigate electronic medical record

Handling Denials

- Request medical peer-to-peer interaction
  - Offer additional information and rationale to discuss with clinical reviewers who made initial determination
  - Must be completed by an MD/NP/PA
- Monitor for trends
  - Increased denials for repetitive reasons may require payer, billing or provider education
- Hold payer accountable
  - Regardless of the size of the organization
    - Example: Payer not recognizing authorization because it came from a third party administrator and denying claims for reason of “lack of pre-certification”

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Medicare

- Most Medicare Administrative Contractors (MAC) have at least one I-O agent Local Coverage Determination (LCD)
- Some MAC have separate LCD for all agents
  - Cigna Government Services (CGS) published atezolizumab LCD within the first six weeks of release of the agent
  - Updated pembrolizumab dosing (Q6W) – Medicare did not reimburse immediately after approval
- Medicare formulary updated quarterly
  - New products or indications may not be reimbursed/covered immediately
- Use of maximum dosages regardless of weight
  - Maximum allowable units per day and per date span for specialty drugs
- No successful reimbursement outside the FDA label indications

Off-label medication process: *Medicare pre-treatment*

1. Before off-label use is considered, a **risk/benefit conversation** (medical, financial risks) needs to occur with the patient
2. If patient and treating physician wish to proceed, IO point person and reimbursement specialist work together to gather **sufficient evidence** for off-label use
3. Have reimbursement specialist **reach out to manufacturer** for options
4. Medication assistance coordinator, reimbursement specialist, and clinical team **determine payment options**
   - Manufacturer assistance/replacement options
   - Medicare payment

Off-label medication process

5. Patient and the team decide **whether to proceed** with off-label use
6. After the patient receives off-label therapy, the **claim is submitted** to Medicare
7. If the claim is not immediately approved, up to **5 levels of appeals** are allowed
8. If claim is ultimately denied, financial counselors arrange for **payment** of the Medicare allowed amount

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  - On-label treatment
  - Off-label treatment
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Commercial Payers

- Policies primarily based upon published scientific evidence, Medicare reimbursement standards, and national guidelines
- Clinical policy guidelines and pathways
  - Vendor Pathways examples: Well Point, New Century Health, AIM
  - Clinical policies examples: Anthem, Aetna, UHC, Cigna, Humana
- Often the clinical policies require medication eligibility restrictions beyond the label and additional criteria to be met in order to assure reimbursement
  - Example: Anthem clinical policies for nivolumab and pembrolizumab include patient's current ECOG score must be 0-2

Commercial Payers

- Use of maximum dosages regardless of weight
  - Maximum allowable units per day and per date span for specialty drugs
- Disproportionate approvals of total billing units versus doses for a specific period of time
  - Example: Authorization for 200 mg pembrolizumab for 6 infusions but date range is for nine months
  - Make sure that the dates and authorizations match
  - Develop process for ensuring new authorization is obtained when old authorization expires

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  - On-label treatment
  - Off-label treatment
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Off-label medication process: *Commercial payers*

1. Before off-label use is considered, a **risk/benefit conversation** (medical, financial risks) needs to occur with the patient.
2. Pharmacist and reimbursement specialist work together to submit **pre-determination request** to payer.
3. If denied, an **appeal** can be filed.
4. If still denied, if there is sufficient evidence for off-label use, reimbursement specialist and medication assistance coordinator **explore payment options**, including contacting manufacturer.

Off-label medication process: *Commercial payers*

5. Patient and team decide **whether to proceed** with off-label use
6. Managed care, reimbursement specialist, and CFO determine the appropriate amount for the **patient to deposit** toward the treatment, or have patient sign **financial responsibility agreement** per institutional policies
7. Patient submits deposit/agreement and **off-label treatment is given**

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- Practical aspects of immunotherapy
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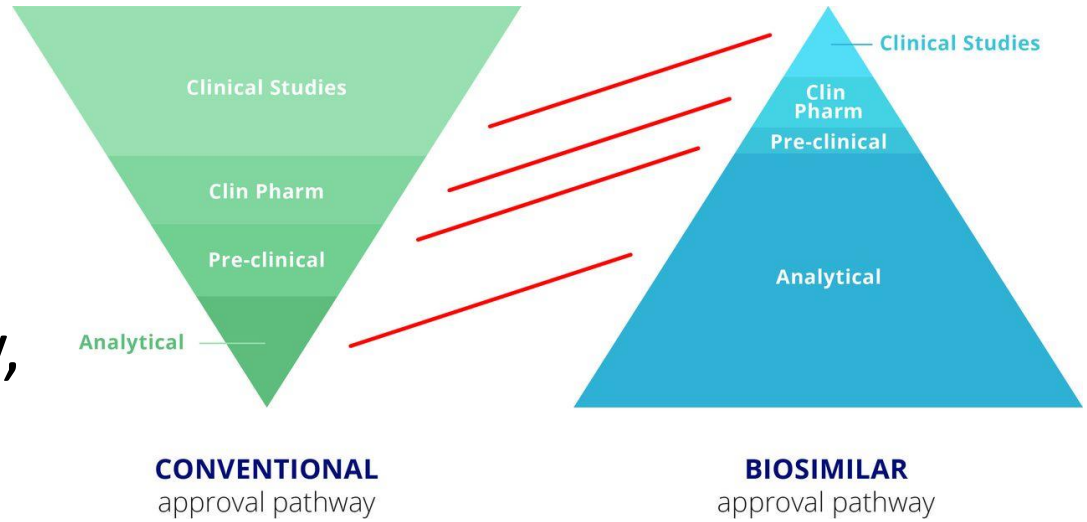
  - Biosimilars
  - Cellular therapies

Biosimilars

- FDA requires biosimilars to be highly similar, but not identical, to reference product
- Has to demonstrate no clinically meaningful differences in efficacy, safety, and potency
- Primarily tested through non-clinical pathways – examining structural and functional nature of the product



Isaacs *et al*, Consid Med 2017.

Biosimilars

- "Biosimilars" is only used to refer to biologic therapies
- Since they are not structurally identical to the reference product, they are not "generics"
- Often approved for same indications as reference product, unless manufacturer still has orphan drug exclusivity or other rights to an indication
  - Example: bevacizumab-awwb approved for CRC, NSCLC, glioblastoma, RCC, and cervical cancer, just like bevacizumab
  - Bevacizumab-awwb not approved for ovarian cancer, since manufacturer has orphan drug exclusivity until 2021

Original "reference product": **bevacizumab**

Non-proprietary drug name

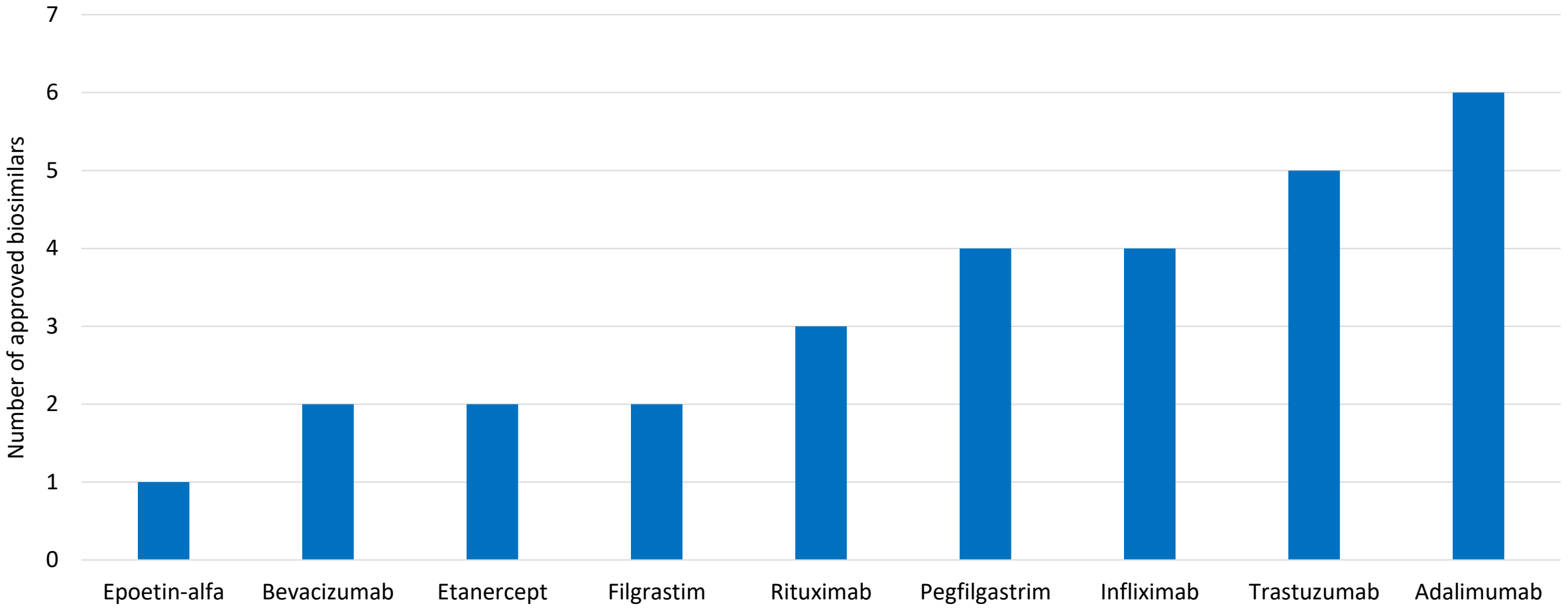
Biosimilar: **bevacizumab-awwb**

Four meaningless lowercase letters, indicating biosimilar agent

Non-proprietary drug name

Pittman, JHOP 2019

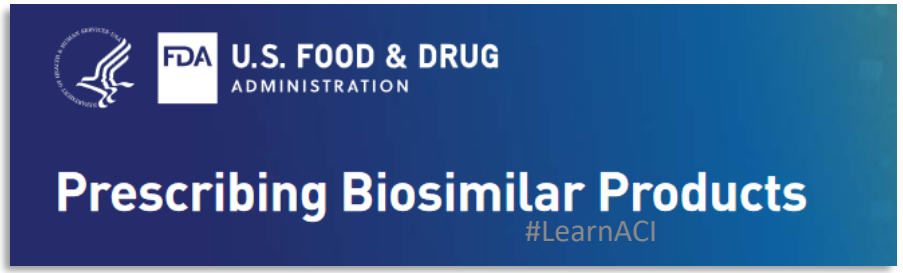
Biosimilars approved by the FDA



FDA Biosimilar Product Information

Biosimilars – practical considerations

- Healthcare providers, pharmacists, and patients are critical for biosimilar acceptance and usage
- Substitution policies vary by state – “interchangeable products” can be substituted without prescriber input
  - Vary by institutional policies (e.g. Pharmacy and Therapeutics committee may approve products to be interchanged by pharmacist without prescriber approval)
- Incentives to prescribe biosimilars from Medicare
- Formulary product (reference or biosimilar) varies by insurance company
  - Pharmacy needs to stock multiple biosimilar products
  - Preferred product may change with limited or no notice



Unique considerations for CAR T therapies

- Large up-front cost instead of smaller costs over time
- Potential side effects can lead to large costs as well
- Financial risks associated with cellular therapies may limit facilities that want to administer them
- Medicare coverage:
  - National coverage determination in August 2019
  - Will be covered by Medicare if administered in health care facilities that follow FDA REMS (risk evaluation and mitigation strategies)

CAR T reimbursement through Medicare

- New Technology Add-On payment expires in September 2020
- CMS has proposed a new DRG for CAR-T therapy for 2021
  - 2020 - DRG 016: Autologous Bone Marrow Transplant with Complications or Major Complications (CC/MCC) or T-Cell Immunotherapy
  - 2021 (proposed) – CRG 018: CAR T-cell immunotherapy

Actual cost of CAR-T administration*	Base DRG 16 payment	Maximum NTAP payment	Outlier payment and other adjustments*	Total DRG payment*	Difference from actual cost in 2020*
$403,000	$43,000	$242,450	$67,550	$353,000	-$50,000
*Average values					

Strohman, American Action Forum 2020.

Future Considerations

- Payer ability to keep up with accelerating evidence-based new indications (e.g., new lines of therapy, new tumor types)
- Increasing utilization of checkpoint inhibitors in combination with a host of agents (e.g., chemo, targeted, immunotherapeutic)
- Potential for coverage policies to be biomarker driven (e.g., PD-L1 overexpression)
- Financial implications of high-dollar agents becoming first line
- Emergence of biosimilars and CAR T treatments