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ADVANCES IN Cancer IMMUNOTHERAPY™

Practical Barriers in Cancer Immunotherapy Treatment

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MUSC Health

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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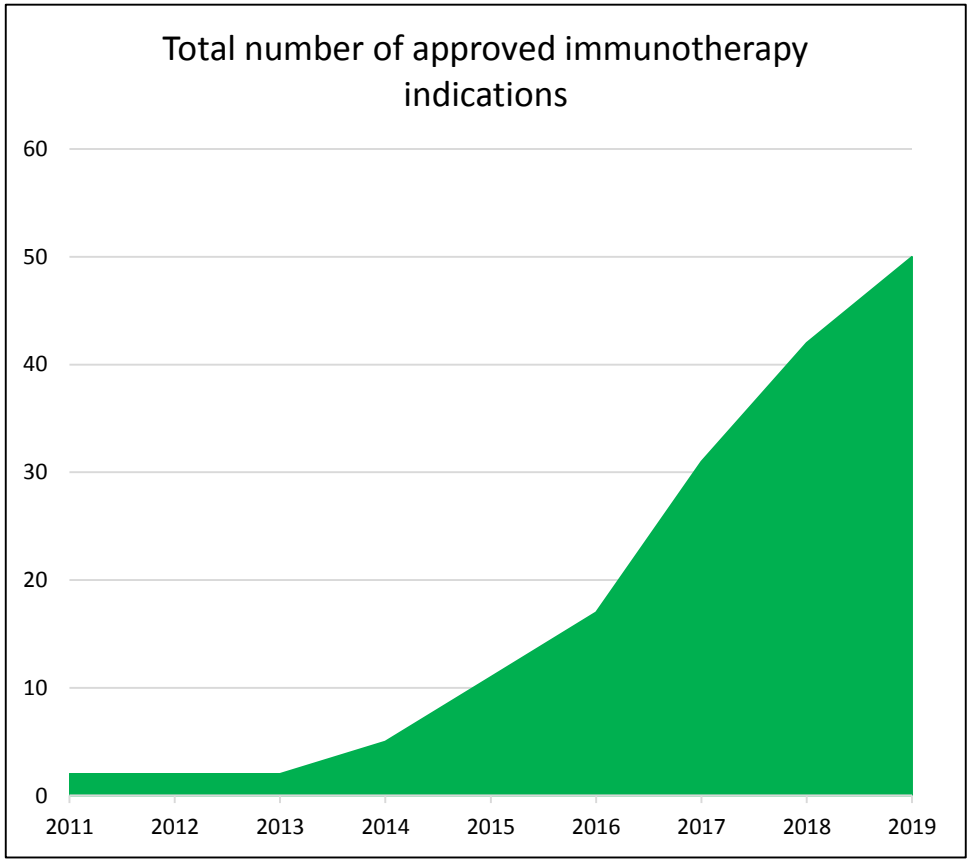
Disclosures

- I have no conflicts of interest to disclose
- I will be discussing non-FDA approved indications during my presentation.
  - In the context of reimbursement and financial assistance programs only

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
- Not only new products, but a myriad of new combinations and regimens



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, advance 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!)

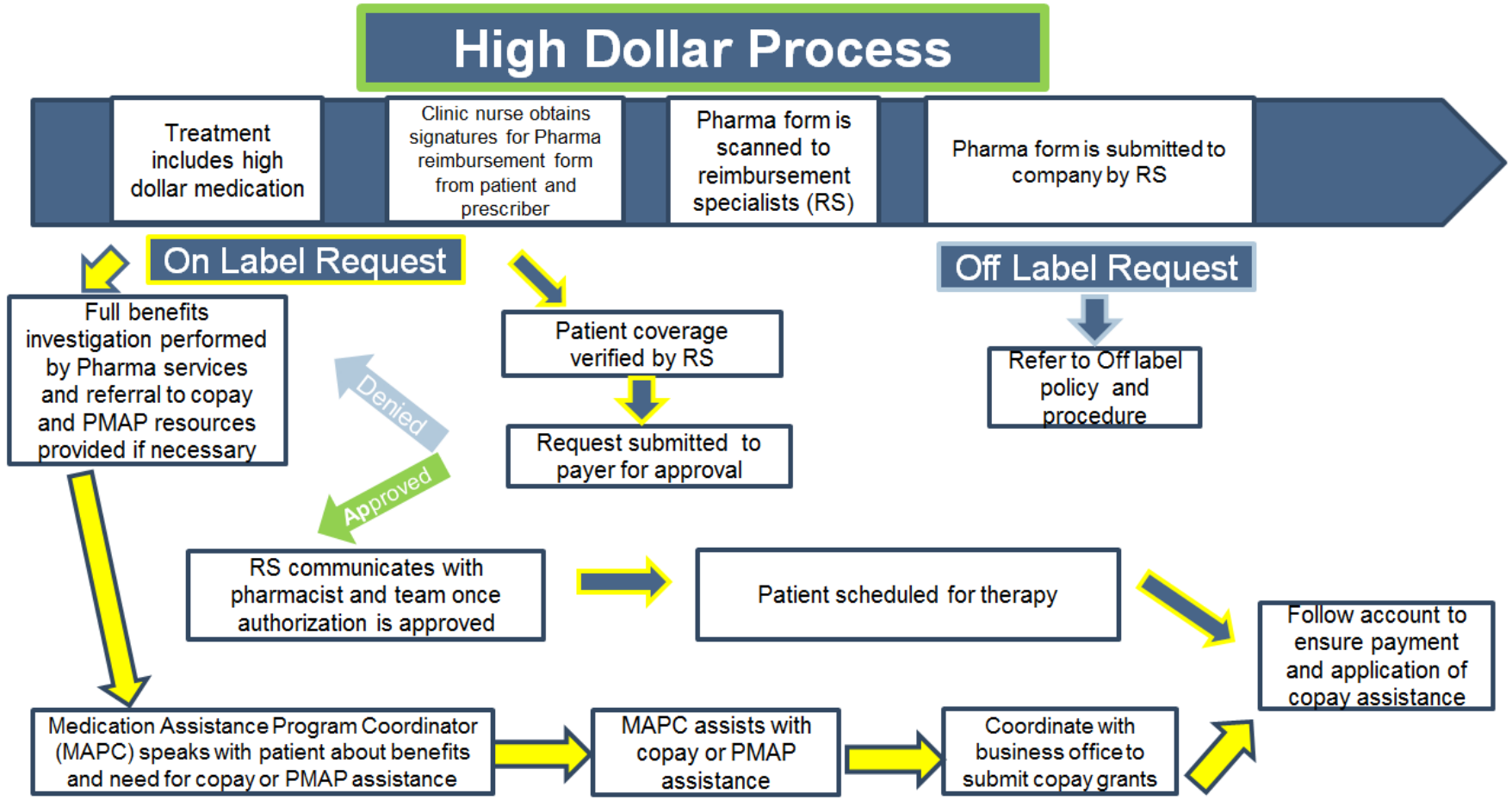
Manage Reimbursement/Finances

- New-to-market I-O agents may not yet have specific J-Code
  - Ensure a process is in place for appropriate management/billing until J-Code is assigned or, in the case of Hospital Outpatient Prospective Payment Services, a C-Code (Temporary = C9399)
- Identify a point person from within your financial or reimbursement staff to focus on I-O agents and understand the nuances of the various patient support programs
  - Manufacturer benefits verification programs, replacement programs, co-pay support programs, co-pay foundations, and patient assistance programs
- Ensure your practice has sufficient Patient Advocacy
  - Most practices have found that Financial Counselors/Medication Assistance Coordinators pay for themselves many times over; if you are not sure if you have enough, it's a good time to conduct an analysis

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 ABN or NONC
  - Peer review process for appeal if needed

High Dollar Process

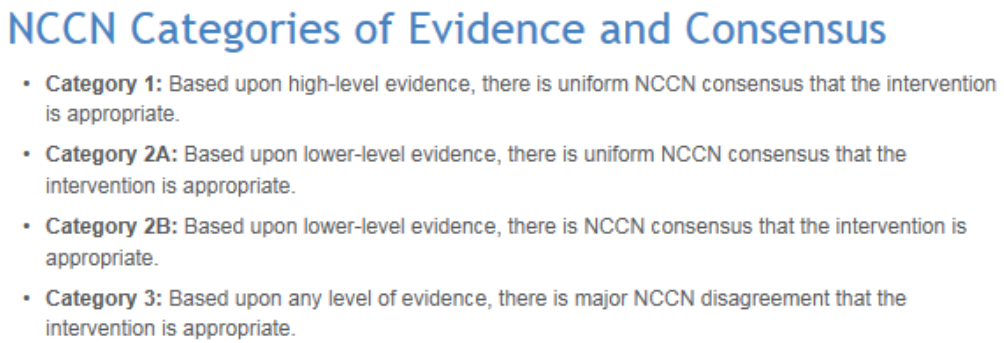


Medicare

- 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
- No successful reimbursement outside the FDA label indications if not in an LCD or National Coverage Determination (NCD)
  - Have had success with working with local MAC to add off-label indications to existing LCDs.
  - Have not been able to add LCDs thus far

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, pharmacist and reimbursement specialist work together to gather **sufficient evidence** for off-label use
    1. Utilize approved Compendia for clinical evidence (NCCN, Micromedex, Clinical Pharmacology, Lexi-Drugs, AMA-DA)
    2. Level 2a evidence or higher for Medical Necessity



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

3. Medication assistance coordinator, reimbursement specialist, and clinical team **determine payment options**
    - Manufacturer assistance/replacement options
    - Medicare payment
4. Patient and the team decide **whether to proceed** with off-label use

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

5. If off-label/does not meet Medicare Medical Necessity, an **Advanced Beneficiary Notice** of Noncoverage (ABN) should be presented to and signed by the patient.
6. After the patient receives off-label therapy, the **claim is submitted** to Medicare (per the ABN)
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

Commercial Payers

- Policies primarily based upon published scientific evidence
- 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 policy for nivolumab includes patient's current ECOG score 0-2 be met

Commercial Payers

- Use of maximum dosages regardless of weight
  - Maximum allowable units per day and per date span for specialty drugs
- Use of National Drug Code (NDC) units versus CPT/Healthcare Common Procedure Coding System (HCPCS) units creates confusion and concern for underpayment
  - J code represents the amount of drug per billing unit
    - 1 J code per medication
    - J code established by CMS
  - NDC represents the manufacturer and size of the vial
    - 1 NDC code for each vial size for each manufacturer
    - NDC code established by FDA and manufacturer
  - Monitor closely for errors in underpayment

Commercial Payers

- Disproportionate approvals of total billing units versus doses for a specific period of time
  - Example: Authorization for 90 mg pembrolizumab for 6 infusions but date range is for nine months - Make sure that the dates and authorizations match
- Always pursue authorization/pre-determination for IO's, regardless of whether the therapy is on or off-label
  - Retrospective denials often occur, particularly for off-label uses, even when there was a pre-determination in acceptance of the use

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.**
    1. Pharma Programs
    2. Grant Programs
    3. Institutional Level Foundation Programs

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
7. Patient submits deposit and **off-label treatment is given**

Commercial and Government Payers

- Billing for waste with immuno-oncology agents
  - Proper usage of the JW modifier
    - JW modifier will indicate the amount of waste volume represented
    - I-O agents that are single-use vials or single-use package for unused portion are eligible
    - Multi-dose vials are not eligible (and currently not available)
  - Not all payers will pay for waste or only pay for part
  - Some payers do not allow rounding of doses and do not pay for waste (a lose/lose situation for institutions)
  - Proper documentation necessary in the medical record for discarded waste
    - Mandated wastage rationale for any JW lines on Medicare claims on January 1, 2017

Dose Rounding/Vial Optimization

- Rounding down to the nearest vial size or billing unit
  - Decrease waste
  - Decrease cost to the patient
- Ensure policy is in place to allow dose rounding and BFW
  - Policy and procedure must outline how waste is to be documented in the chart (dropping a charge from the pharmacy is acceptable)
  - Exceptions can be listed to allow billing for waste from Automated Dispensing Cabinets (outside the pharmacy)

Denials – Common Reasons

- Lack of pre-certification or authorization
- Medical necessity
- 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

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
- 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
- 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”

Handling Denials

- Challenge outdated payer policies
  - Develop reconsideration packet (for both commercial payer and Medicare) with evidence to support addition of covered diagnoses and/or regimens excluded from payer policies

Practical barriers beyond payment

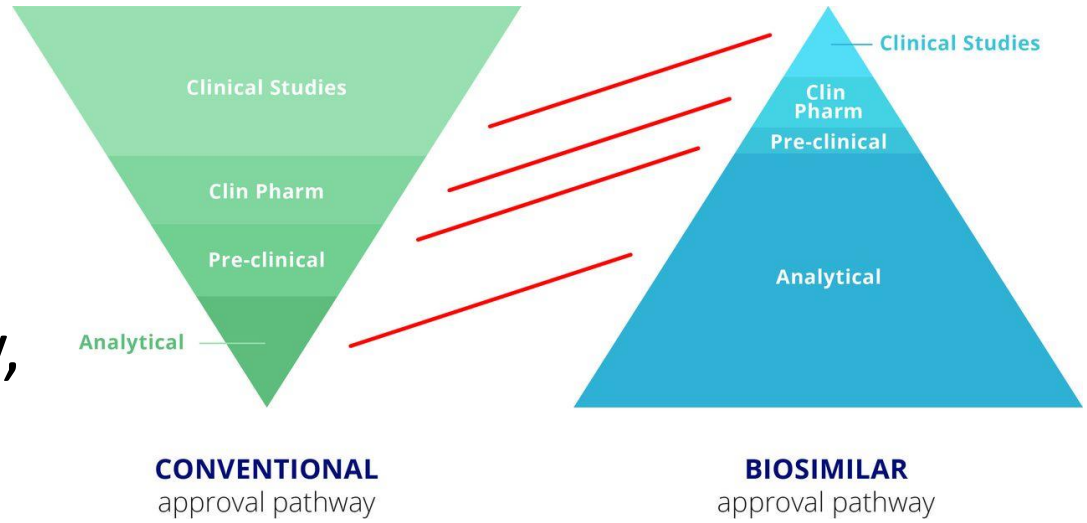
- IO-related medical emergencies
- Biosimilars
- CAR T treatments

IO Management Strategies

- Develop protocols
  - Use your “I-O Champion” to take the lead in developing/revising any treatment protocols that may be impacted by the addition of new I-O therapies in your practice
- Patient education
  - Educate all patients on an I-O therapy to clearly identify themselves as such; make sure that these patients can be quickly identified as being on an I-O therapy in their medical record
- Staff education
  - Ensure staff understand and can identify the most common adverse events associated with I-O products, and know when these events could be potentially be life-threatening and/or require immediate clinical attention

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 approved by the FDA

NOTE Not all products commercially available

Biosimilar	Reference Product	Approval Date
Inflectra (infliximab-dyyb)	Remicade (infliximab)	April 2016
Erelzi (etanercept-szzs)	Enbrel (etanercept)	August 2016
Amjevita (adalimumab-atto)	Humira (adalimumab)	September 2016
Renflexis (infliximab-abda)	Remicade (infliximab)	May 2017
Cyltezo (adalimumab-adbm)	Humira (adalimumab)	August 2017
Ixifi (infliximab-qbtx)	Remicade (infliximab)	December 2017
Retacrit (epoetin alfa-epbx)	Procrit (epoetin alfa)	May 2018
Hyrimoz (adalimumab-adaz)	Humira (adalimumab)	October 2018

Cancer-Related Biosimilars Approved by the FDA

NOTE Not all products commercially available

Cancer-related Biosimilar	Reference Product	Approval Date
Zarxio (filgrastim-sndz)	Neupogen (filgrastim)	March 2015
Mvasi (bevacizumab-awwb)	Avastin (bevacizumab)	September 2017
Ogivri (trastuzumab-dkst)	Herceptin (trastuzumab)	December 2017
Fulphilia (pegfilgrastim-jmdb)	Neulasta (pegfilgrastim)	June 2018
Nivestym (filgrastim-aafi)	Neupogen (filgrastim)	July 2018
Truxima (rituximab-abbs)	Rituxan (rituximab)	November 2018
Udenyca (pegfilgrastim-cbqv)	Neulasta (pegfilgrastim)	November 2018
Herzuma (trastuzumab-pkrb)	Herceptin (trastuzumab)	December 2018

Cancer-related Biosimilar	Reference Product	Approval Date
Ontruzant (trastuzumab-qyyp)	Herceptin (trastuzumab)	January 2019
Trazimera (trastuzumab-qyyp).	Herceptin (trastuzumab)	March 2019
Eticovo (etanercept-ykro)	Enbrel (etanercept)	April 2019
Kanjinti (trastuzumab-anns)	Herceptin (trastuzumab)	June 2019
Zirabev (bevacizumab-bvzr)	Avastin (bevacizumab)	June 2019
Ruxience (rituximab-pvvr)	Rituxan (rituximab)	July 2019
Ziextenzo (pegfilgrastim-bmez)	Neulasta (pegfilgrastim)	November 2019

Last Updated 1/30/20

Purple Book Link

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
- Incentives to prescribe biosimilars from Medicare

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
- 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)
  - May be covered for off-label indications

"Local Practices"

- EHR Limitations
  - Optimal workflow for patient scheduling not achieved due to EHR limitations, and large organizational structure complexity
- Staff Training
  - Pre-certification team training for using LCDs and Compendia as part of the authorization process.
- Co-Pay Assistance
  - Based on your workflow/organizational structure, co-pay assistance can be challenging to implement
- Medication Assistance Programs (Drug Replacement and Free Drug)
  - Pharmacy Technician-based program
- Denials/Appeals
  - Pharmacists can help write appeal letters, do peer-to-peers in some cases, and provide alternative therapy recommendations based on coverage.
  - Much success with getting approvals with off-label indications, or free drug after a denial.

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 agents becoming first line
- Emergence of biosimilars and CAR T treatments