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Chapter 17 Case Study

Part 1

Meet the Patient

Figure 1. A picture of Kevin Thompson. This image was created using AI.

Kevin Thompson, a 52-year-old construction manager, lives in a quiet suburban neighborhood with his wife, Tami, and their two teenage sons.

Kevin has a reputation as a hardworking problem-solver who thrives outdoors, often hiking with his family or working on home improvement projects during weekends. Despite his active lifestyle, Kevin has a history of mild hypertension managed with medication.

The First Signs of Trouble

About six months ago, Kevin noticed a persistent dry cough and attributed it to seasonal allergies. Over time, he developed fatigue, shortness of breath, and an unintentional weight loss of 12 pounds. Tami insisted he see a doctor when his symptoms prevented him from enjoying their usual hikes.

Part 2

Visit to the Clinic

Kevin's primary care physician ordered a chest X-ray.

Figure 2. X-ray procedure; Image source: NIH National Cancer Institute (https://visualsonline.cancer.gov/)

A mass was found in his upper-left lobe.

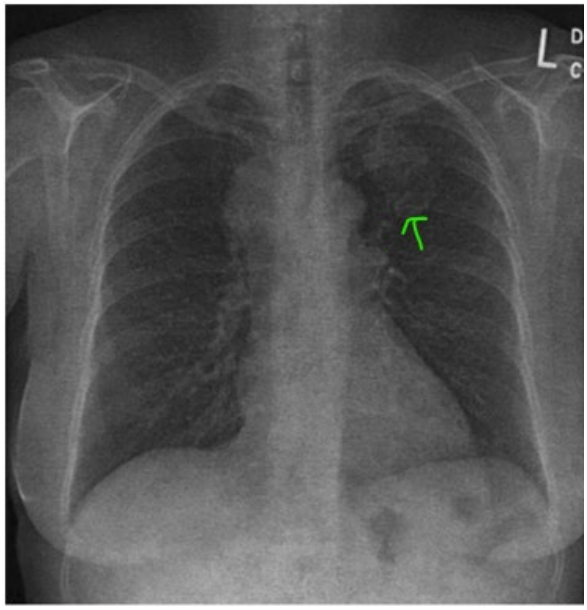

Figure 3. Image of chest x-ray with arrow pointing to a mass; Image source: McGraw Hill Access Medicine (https://accessmedicine.mhmedical.com/)

This prompted further evaluation, including a CT scan, biopsy of the mass, and bloodwork.

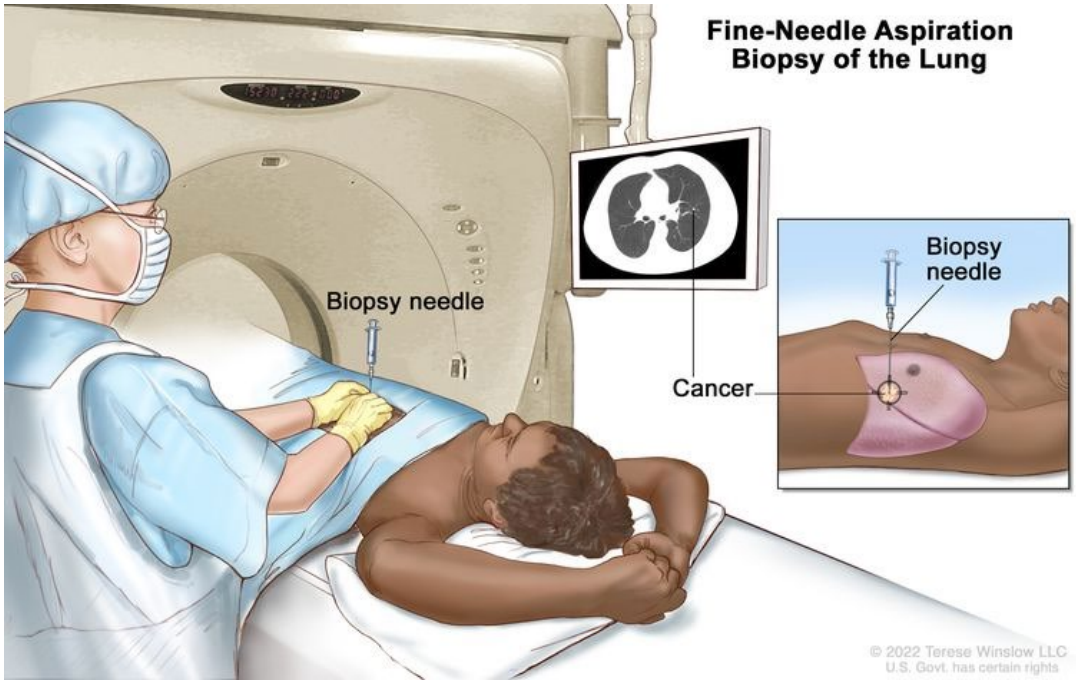

Figure 4. Procedure of CT scan and biopsy; Image source: NIH National Cancer Institute (https://visualsonline.cancer.gov)

Figure 5. Image of CT scan of lung with an arrow pointing to mass; Image source: McGraw Hill Access Medicine (https://accessmedicine.mhmedical.com/)

Table 1. Complete blood count results.

Test	Result	Reference Range
Hgb	11.2 g/dL	13.5–17.5 g/dL
Hct	35%	41–53%
Plt	400,000/µL	150,000–450,000/µL
WBC	12,000/µL	4,500–11,000/µL
Neutrophils	70%	40–70%
Lymphocytes	18%	20–40%
Monocytes	9%	2–8%
Eosinophils	2%	1–4%
Basophils	1%	0-1%

Question 1. Kevin's CBC showed mild anemia and slightly elevated monocytes. What is the most likely explanation for these findings in the context of cancer?

A. Reduced oxygen delivery from anemia is causing compensatory immune activation, increasing monocyte levels.

B. The tumor's immunosuppressive microenvironment increases monocyte production to inhibit lymphocyte activity.

C. Tumor-induced bone marrow suppression leads to anemia and monocyte activation.

D. Chronic inflammation induced by the tumor results in anemia of chronic disease and elevated monocytes. (Correct answer)

Question 2. Which immune system function is most relevant to detecting and eliminating abnormal cells like those seen in cancer?

A. Production of antibodies by B cells

B. Activation of T helper cells

C. Immune surveillance by NK and CTL cells (Correct answer)

D. Cytokine release by macrophages

Diagnosis

A biopsy of the lung mass revealed non-small cell lung cancer (NSCLC). Because the tumor was between 3.0-4.0 cm, it was classified as Stage IB.

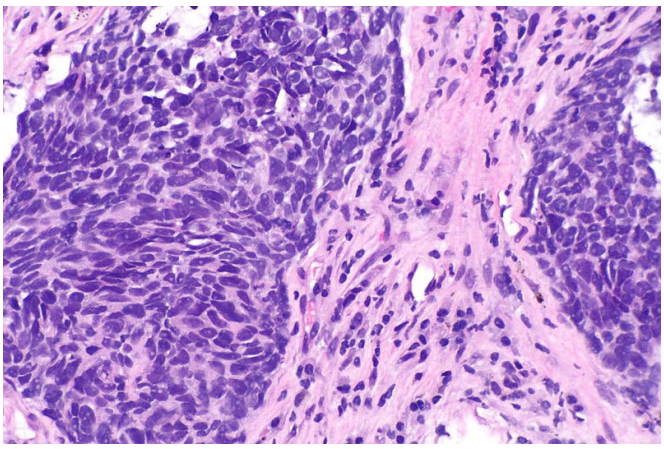

Figure 6. Histology slide of lung tissue mass; Image source: Librepath, CC BY-SA 3.0 https://creativecommons.org/licenses/by-sa/3.0 via Wikimedia Commons

NSCLC is the most common type of lung cancer, accounting for about 85% of all lung cancer cases. It is a broad category of lung cancers that differ from the less common small cell lung cancer (SCLC) in terms of growth patterns, behavior, and treatment options.

NSCLC originates in the epithelial cells lining the respiratory tract. It is characterized by uncontrolled growth of abnormal cells in the lungs, which can invade nearby tissues and spread (metastasize) to other parts of the body.

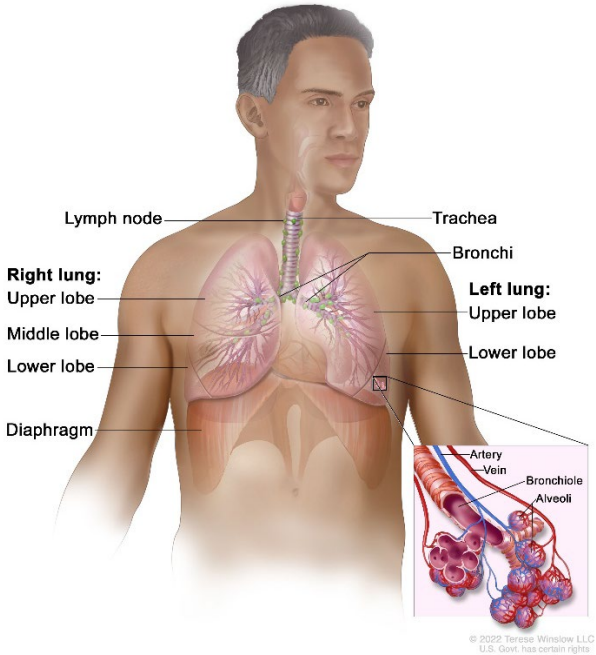

Figure 7. Anatomy of the respiratory system, including a lymph node; Image source: NIH National Cancer Institute (https://visualsonline.cancer.gov)

There are several types of non-small cell lung cancer, differing in the type of cell that becomes cancerous. The cancer cells of each type grow and spread in different ways.

- Adenocarcinoma (40% of NSCLC cases)
  - Originates in mucus-producing glandular cells that line the alveoli.
  - Most common type in non-smokers and individuals with a history of light smoking.
- Squamous Cell Carcinoma (25–30% of NSCLC cases)
  - Begins in the flat cells lining the airways.
  - Strongly associated with smoking.
- Large Cell Carcinoma (10–15% of NSCLC cases)
  - May begin in several types of large cells.
  - Tends to grow and spread more quickly than other NSCLC subtypes.
- Less common types of non-small cell lung cancer include adenosquamous carcinoma, sarcomatoid carcinoma, salivary gland carcinoma, carcinoid tumor, and unclassified carcinoma.

Question 3. A biopsy of an NSCLC tumor reveals flat, keratinizing epithelial cells under a microscope. What is the most likely diagnosis?

A. Adenocarcinoma

B. Large cell carcinoma

C. Squamous cell carcinoma (Correct answer)

D. Small cell lung cancer

NSCLC disrupts normal lung function by replacing healthy tissue with tumor tissue. This can:

- Impair oxygen exchange in the lungs, leading to symptoms like shortness of breath and fatigue.
- Cause systemic symptoms, such as weight loss, due to the release of inflammatory molecules and cytokines.
- Spread to regional lymph nodes, the brain, bones, or liver, causing additional complications.

Symptoms often include:

- Persistent cough (often with blood-tinged sputum)
- Shortness of breath
- Chest pain
- Unexplained weight loss
- Fatigue
- Hoarseness or voice changes

These symptoms may overlap with other conditions, making early diagnosis challenging.

Question 4. What is the clinical significance of distinguishing between the subtypes of NSCLC?

A. All NSCLC subtypes respond equally to chemotherapy, so subtyping has minimal relevance.

B. Subtypes like squamous cell carcinoma are excluded from immunotherapy, so subtyping limits treatment options.

C. Subtyping determines the stage of cancer, which is the only factor influencing treatment decisions.

D. Subtyping helps guide treatment decisions, such as the use of targeted therapies or immunotherapies. (Correct answer)

Part 3

Exploring Treatment Options

NSCLC treatment depends on the stage of cancer and includes:

1. **Surgery:** Removal of the tumor for localized NSCLC.
2. **Radiation Therapy:** Targets and destroys cancer cells in specific areas.
3. **Chemotherapy:** Kills rapidly dividing cells but has systemic side effects.
4. **Targeted Therapy:** Drugs like EGFR inhibitors for specific mutations.
5. **Immunotherapy:** Checkpoint inhibitors for cancers expressing high levels of PD-L1.

Kevin's oncologist explained that for his type of cancer, the best approach would be to make a two-stage treatment plan:

1. Surgery - wedge resection
2. Targeted Therapy or Immunotherapy

The first objective of treatment would be to remove the tumor via wedge resection of the lung. In this procedure, a triangle-shaped slide of tissue is removed. This section contains the tumor and a small amount of normal tissue around it.

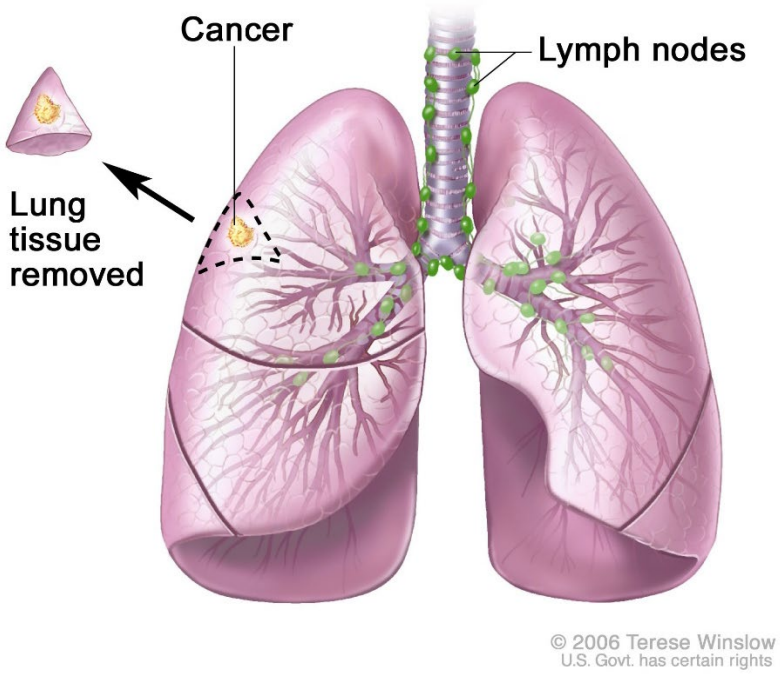

Figure 8. Wedge resection of the lung; Image source: NIH National Cancer Institute (https://visualsonline.cancer.gov)

The second objective of treatment would be to remove any remaining cancer cells from the body and produce a lasting immune response against any reemerging cancer cells.

The decision to use either targeted therapy or immunotherapy depends on the genetic profile of the cancer cells.

Molecular testing is performed to identify actionable genetic mutations in the tumor. These mutations can determine the best course of treatment, especially in advanced or metastatic.

Testing on the cells from the biopsy showed no Epidermal Growth Factor Receptor (**EGFR**) or Anaplastic Lymphoma Kinase (**ALK**) mutations.

Mutations in the EGFR gene can lead to uncontrolled cell growth and are common in some types of NSCLC, particularly in non-smokers and adenocarcinoma patients. Tumors with EGFR mutations often respond to targeted therapies such as EGFR inhibitors.

ALK rearrangements involve a fusion of the ALK gene with another gene, creating a protein that drives tumor growth. These rearrangements are less common but are significant because they make tumors susceptible to ALK inhibitors.

Testing did show that the cancer cells had a high expression of **PD-1L**.

Question 5. Match each drug name to the correct cancer treatment modality.

Prompt	Answer
Cisplatin	Chemotherapy
Pembrolizumab	Immunotherapy
Osimertinib	Targeted Therapy
Nivolumab	Immunotherapy
Erlotinib	Targeted Therapy
External Beam Therapy	Radiation Therapy

After surgery to remove the tumor, Kevin was started on pembrolizumab infusions every three weeks.

Pembrolizumab is a type of targeted therapy drug called an immune checkpoint inhibitor (a type of immunotherapy). It is a monoclonal antibody that binds to the protein PD-1 on the surface of immune cells called T cells.

It works by keeping cancer cells from suppressing the immune system. This allows the immune system to attack and kill the cancer cells.

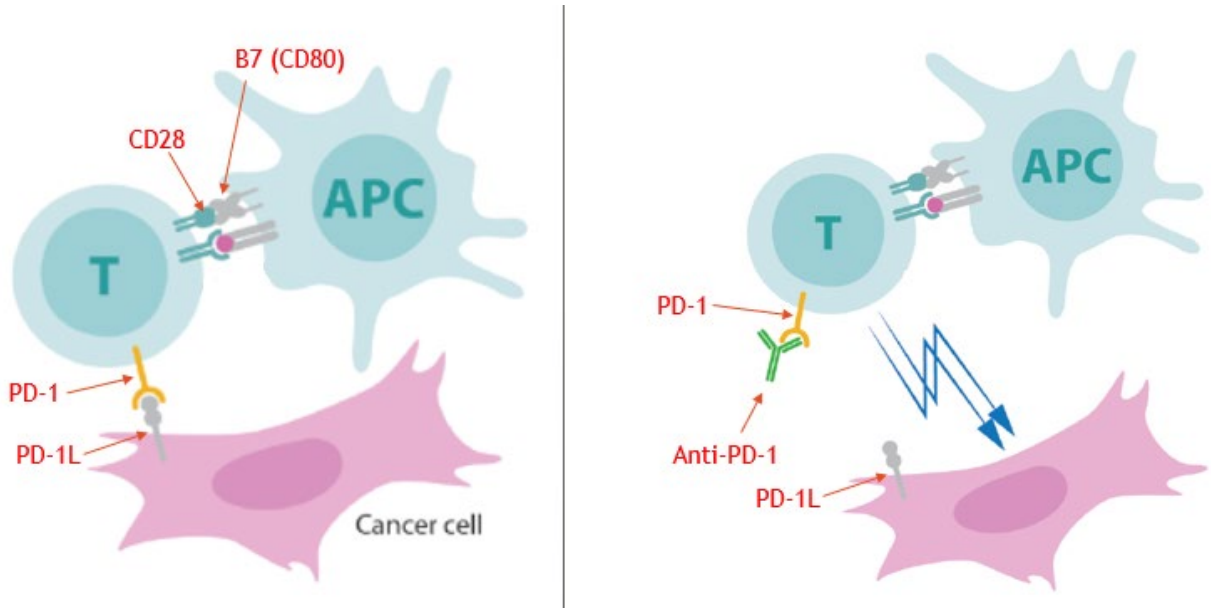

Figure 9. Mechanism of action of PD-1 inhibition; Image adapted from: https://www.nobelprize.org/prizes/medicine/2018/press-release/

After three months, imaging showed a significant reduction in tumor size. By six months, there was no evidence of active tumor metabolism.

Despite mild side effects, including fatigue and a transient rash, Kevin responded well to treatment. His CTLs, now fully activated, targeted and eliminated cancer cells efficiently. Regular monitoring ensured no recurrence of the tumor.

Question 6. What is the role of MHC molecules in immune surveillance?

A. Presenting tumor-associated antigens to activate T cells (Correct answer)

B. Blocking the activity of natural killer cells

C. Suppressing cytokine release in the tumor microenvironment

D. Enhancing antibody production

Question 7. What is the role of PD-L1 in immune evasion by tumors?

A. Enhances MHC presentation to avoid detection

B. Inhibits T cell activation by binding to PD-1 (Correct answer)

C. Suppresses cytokine production in cancer cells

D. Activates NK cells to attack the tumor

Question 8. Kevin's case highlights how molecular testing influences cancer treatment. Which of the following best explains why Kevin's tumor lacking EGFR or ALK mutations shifted the treatment focus to pembrolizumab?

A. EGFR and ALK mutations are biomarkers for immunotherapy effectiveness.

B. Without these mutations, chemotherapy is less effective, requiring alternative strategies.

C. High PD-L1 expression suggests that immune evasion plays a key role, making checkpoint inhibitors appropriate. (Correct answer)

D. Tumors without EGFR or ALK mutations cannot metastasize and are treated with immunotherapy.

Immunotherapy & Personalized Medicine

Personalized medicine, also called precision medicine, is a transformative approach to healthcare that tailors treatment to the individual characteristics of each patient. Unlike traditional one-size-fits-all treatments, personalized medicine considers factors such as a patient's genetic makeup, lifestyle, environment, and the specific molecular characteristics of their disease.

In cancer care, personalized medicine focuses on identifying unique genetic mutations, biomarkers, and pathways that drive tumor growth. These insights allow doctors to select treatments that target the specific biology of the cancer, minimizing harm to healthy cells and maximizing therapeutic success.

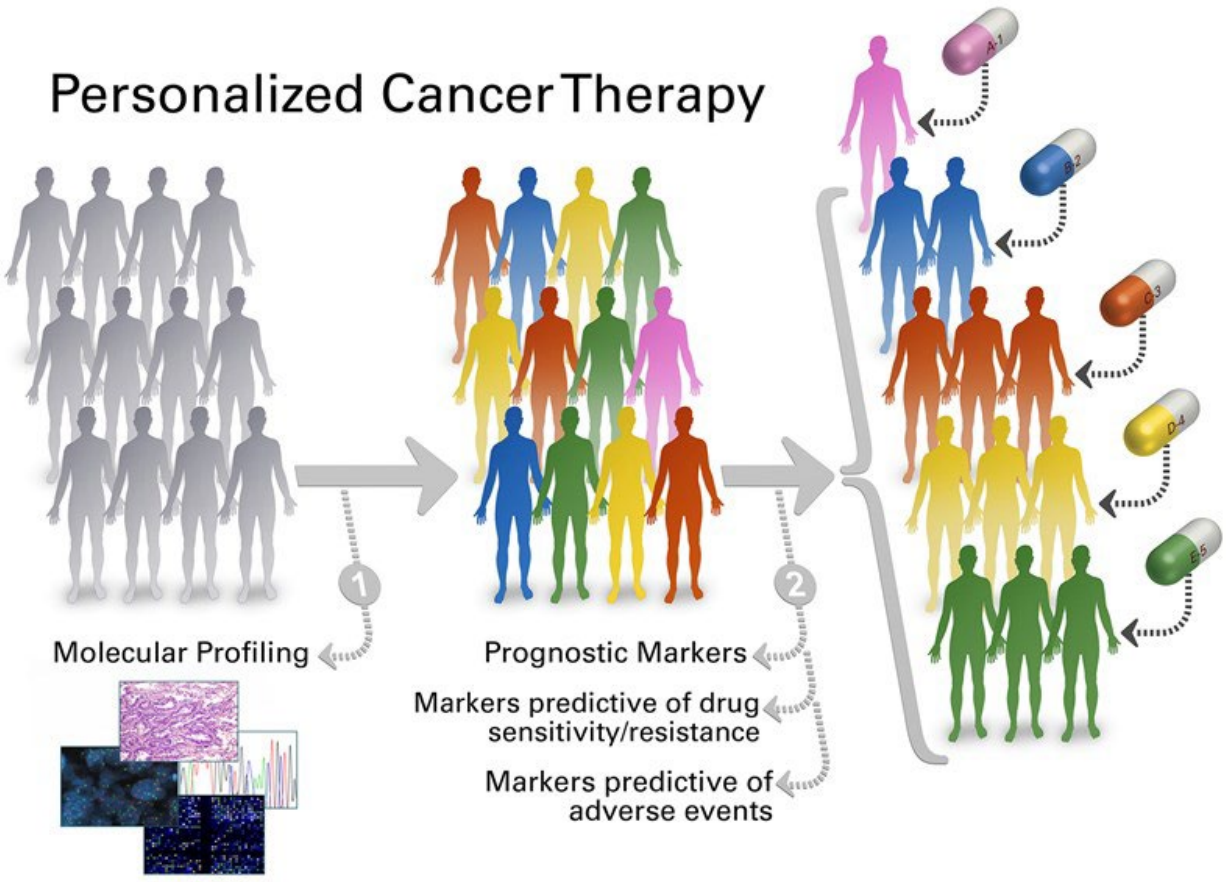

Figure 10. Diagram summarizing personalized cancer therapy; Image source: The University of Texas MD Anderson Cancer Center (https://pct.mdanderson.org/#/)

Key Features of Personalized Medicine:

- Molecular Profiling
  - Analyzing genetic and molecular alterations in the tumor to identify actionable targets.
  - Example: Testing for EGFR mutations or ALK rearrangements in non-small cell lung cancer (NSCLC).
- Biomarker Testing
  - Measuring biomarkers, such as PD-L1 expression, to predict how a patient will respond to certain treatments.
  - Biomarkers guide decisions about whether a patient might benefit from targeted therapies, chemotherapy, or immunotherapy.
- Patient-Centric Approach
  - Customizing treatment to maximize efficacy while reducing unnecessary side effects.
  - Monitoring patient response and adjusting treatment plans accordingly.

Question 9. Immunotherapy and targeted therapies both play roles in personalized cancer treatment. Which scenario demonstrates how immunotherapy integrates into personalized medicine?

A. Prescribing CAR-T therapy to patients whose tumor cells express unique tumor-specific antigens. (Correct answer)

B. Using pembrolizumab for patients with EGFR mutations to block immune suppression.

C. Treating all lung cancer patients with immune checkpoint inhibitors regardless of PD-L1 status.

D. Combining radiation and immunotherapy to target tumors without considering biomarker expression.

Immunotherapy represents a paradigm shift in cancer treatment, leveraging the body's own immune system to fight cancer.

Its role in personalized medicine lies in its ability to target the unique ways a tumor interacts with and evades the immune system.

Immune checkpoint inhibitors, like pembrolizumab, nivolumab, and atezolizumab, block proteins such as PD-1, PD-L1, or CTLA-4 that suppress T cell activity.

Biomarker: PD-L1 expression on tumor cells is used to identify patients likely to benefit from these drugs.

Kevin's case highlights how high PD-L1 expression made him an ideal candidate for pembrolizumab, a therapy tailored to his tumor's immune profile.

Question 10. Why are immune checkpoint inhibitors effective in patients with high PD-L1 expression?

A. They block PD-L1, enhancing antigen presentation on tumor cells

B. They inhibit PD-1, restoring T cell activation and cytotoxic function (Correct answer)

C. They suppress NK cell activity, reducing immune suppression

D. They enhance antibody production against tumor-associated antigens

Benefits of Personalized Immunotherapy include the following:

- Enhanced Precision: Treatments like checkpoint inhibitors are used only when biomarkers indicate a high likelihood of response.

- Minimized Side Effects: By targeting specific pathways or mechanisms, personalized immunotherapy reduces the off-target toxicity seen in traditional therapies.
- Durable Responses: Immunotherapies can lead to long-term remission by reactivating the immune system for sustained surveillance.

Advances in genomics, proteomics, and artificial intelligence are further refining the integration of immunotherapy into personalized medicine

Question 11. Which of the following is a key benefit of personalized medicine in cancer treatment?

A. It eliminates the need for chemotherapy by focusing solely on immunotherapy.

B. It ensures that all patients receive the same treatment regardless of their tumor profile.

C. It tailors treatments based on molecular and genetic profiling, increasing efficacy, and reducing unnecessary side effects. (Correct answer)

D. It replaces the need for biomarker testing, as all cancers respond equally to personalized approaches.

Question 12. Which of the following is a significant ethical concern associated with personalized medicine in cancer treatment?

A. Personalized medicine increases the risk of systemic side effects compared to traditional therapies.

B. Personalized medicine discourages the development of new biomarkers and targeted therapies.

C. Patients undergoing personalized medicine are not required to provide informed consent for genetic testing.

D. Access to personalized treatments may be limited by socioeconomic disparities, leading to unequal outcomes. (Correct answer)

Life After Cancer

Two years later, Kevin remains cancer-free and enjoys an active lifestyle. Regular follow-up scans and bloodwork ensure early detection of any recurrence.

Kevin's case highlights the importance of personalized medicine and leveraging immunological advances to achieve long-term remission.

Kevin often reflects on his journey, sharing his story with others facing similar diagnoses. His case exemplifies how modern immunotherapy integrates principles of immune activation and tumor biology to offer patients new hope.