Title:

How can we effectively integrate emerging immunotherapies and targeted therapies into existing treatment protocols to improve patient outcomes?

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State:
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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Improving patient outcomes in oncology requires the successful integration of new immunotherapies and targeted medicines into current therapy regimens. By combining the best features of both strategies, this integration could result in more individualized and efficient cancer treatments.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):

A)

1. Immunotherapy Efficiency: Useful for tumors with many mutations (for example, lung and melanoma); some patients have long-term benefits.
2. Selective Treatment: very impressive in the treatment of malignancies that are genetically specified (e.g., *EGFR*-mutant lung cancer, HER2-positive breast cancer).
3. Advantages: Immunotherapy: Enhances the rate of survival, decreases the possibility of recurrence, and is efficient on various types of cancer. Apart from this, precise treatment of cancer cells through targeted therapy, lower has side effects, and speedy the response of the patients.
4. Limitations: Immunotherapy: Its cost is quite expensive, immune-related side effects; response rates are variable.
5. Targeted therapy: Determine genetic information through genetic testing, acquire drug resistance over time and the treatment is costly.

B)

Biomarkers for Immunotherapy

1. Expression of PD-L1: A prediction of a positive response to immunotherapy with the drugs, such as pembrolizumab.
2. Tumor Mutational Burden (TMB): Having high TMB in the blood of the patients is related to a higher frequency of them responding to immunotherapy treatment.
3. Microsatellite Instability (MSI-H/dMMR): Indicates that the patient may benefit from immune checkpoint inhibitors. Biomarkers for Targeted Therapy

Biomarkers for Chemotherapy Response

4. *TP53* Mutation: It is connected with the bad outcome of a conventional chemotherapy treatment.

Biomarkers for Hormone Therapy

5. Estrogen & Progesterone Receptors (ER/PR): This may be a decider for the hormonal therapy in breast cancer.
6. Androgen Receptor (AR): Is used in prostate cancer treatment decisions.

C)

1. High Price and Limited Availability: Most of the individuals are incapable of meeting the high and thus unaffordable cost of the drugs or the insufficient insurance coverage. It turns out that it is only specialist cancer clinics located in urban areas that can get it.
2. Patients' Diversity: The personalized approach that is driven by biomarker is obligatory due to the unequal reaction of the patients. The progress of a treatment may be different depending on the heterogeneity of the gene connected with the tumor.
3. The Growth of Resistance: Acquired resistance is not rare if the therapy is directed but it could be due to point mutations in *EGFR, ALK*. The changes in the tumor immune escape pathways can lead to the development of resistance to immunotherapy.
4. Over usage and toxicities of Immunotherapy:

Endocrinopathies, colitis, and pneumonitis are being induced by both drugs, interferon, and cytokine.
Targeted Treatment: toxicities that are off-target and impact organs such as the skin, liver, and heart. Both unique testing and a high level of professionalism are needed. Moreover, the analysis also partly depends on the sophisticated biomarkers and molecular testing, which are expensive and not found everywhere as well. To select the right treatment and suitably control side effects, one needs expertise from specialized oncologists.

D)

1.Managing Toxicities and Side Effects:

- Early Monitoring & Intervention: Toxicities can be recognized at a very early stage with options like simple lab testing, imaging, and listening to the patient's complaint for symptom tracking.
- Multidisciplinary Approach: Consult teams of professionals such as dermatologists, pulmonologists, oncologists and, endocrinologists to address side-effects.
- Patient Education & Awareness: Patient education must focus on training the patient for symptom identification and then the patient's early report of the symptoms to the healthcare provider.

2. Expanding Access to Specialized Testing & Expertise

- Increasing the Number of Biomarker Testing Facilities: Building local laboratories for diagnosis of regional molecular testing
- Government & Industry Collaboration: Grants, Subsidies, and public-private partnerships for Testing Cost-sharing to Lower Costs
- Telemedicine & Remote Consultation: Professional consulting through digital platforms in areas lacking services

3. Reducing Treatment Costs:

- Increasing the Use of Biosimilars & Generic Drugs: The local manufacture of some drugs would contribute to a small cost of the medication
- Insurance & Government Support: Provide the costs of immunotherapy and targeted drugs in public insurance and thus get financial support from the government.
- Risk-Based Pricing Models: The cost of the treatment will depend on the patient's response to medical treatment.

4. Substance Abuse Treatment:

- Combination therapies are strategies to break through drug resistance. These methods include combining immunotherapy with targeted therapy or chemotherapy.
- Adaptive Treatment Strategies: The doctor may endeavor to change drugs in a less stressful way by following a regular research-based molecular profiling protocol.
- Research on Newer Biomarkers: To develop medicine, the latest technology is run to find milder predictors to show which patients may recover. A combination of early detection, better access to healthcare, cost reduction, and innovative treatment options are the essential factors that contribute to maximizing the benefits of immunotherapy and targeted therapy uptake by all patients.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Primary Outcomes of Integrating Emerging Therapies:
1. Improved Survival & Quality of Life: Enhanced progression-free survival (PFS) and overall survival (OS) through biomarker-guided selection of immunotherapies (e.g., PD-L1/TMB) and targeted therapies (e.g., *EGFR/ALK* inhibitors), reducing trial-and-error treatment.
2. Expanded Access: Equitable availability via tiered pricing, local manufacturing, and subsidized biomarker testing (e.g., mobile MSI-H labs in rural areas).
3. Optimized Toxicity & Resistance Management: Reduced severe adverse events (e.g., irAEs) through clinician training programs and next-gen therapies (e.g., *KRAS* inhibitors).
Impact: Precision-driven, equitable, and sustainable cancer care that adapts to evolving science and patient needs.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Effectiveness, Advantages, and Challenges of Immunotherapies & Targeted Therapies
1. Immunotherapies (e.g., PD-1/PD-L1 inhibitors, CAR-T):
a) Effectiveness: Durable responses in melanoma, NSCLC, Hodgkina lymphoma.
b) Advantages: Long-term remission, fewer cumulative toxicities vs. chemotherapy.
c) Challenges: High cost, immune-related adverse events (e.g., colitis), variable response rates (10%-40%).
2. Targeted Therapies (e.g., *EGFR/ALK* inhibitors, *PARP* inhibitors):
a) Effectiveness: High response rates in mutation-driven cancers (e.g., *EGFR*+ NSCLC, HER2+ breast cancer).
b) Advantages: Precision action, lower off-target toxicity.
c) Challenges: Rapid resistance (e.g., T790M in *EGFR*), limited applicability without biomarkers.

Biomarkers for Therapy Decision-Making
1. Immunotherapy Biomarkers:
a) PD-L1 expression, tumor mutational burden (TMB), microsatellite instability (MSI-H).
b) Emerging: Gut microbiome diversity, IFN-ϒgene signature.
2. Targeted Therapy Biomarkers:
a) *EGFR, ALK, ROS1* (lung cancer); *BRCA1/2* (ovarian cancer); HER2 (breast/gastric cancer).
b) Liquid biopsies for resistance mutations (e.g., *EGFR* T790M).

Challenges in Utilization
1. Access & Cost: Limited availability in LMICs; high prices (e.g., CAR-T: $500,000+).
2. Biomarker Testing Gaps: Lack of NGS/immunohistochemistry in rural areas.
3. Toxicity Management: Requires specialized training (e.g., steroid-refractory colitis).
4. Resistance: Acquired mutations (e.g., KRAS in colorectal cancer).
5. Combination Complexity: Synergy with chemo/radiation lacks standardized protocols.
6. Ethnic Variability: Differential efficacy/safety (e.g., higher irAEs in Asians).

Solutions to Address Challenges
1. Cost & Access:
a) Tiered pricing, compulsory licensing, and local manufacturing partnerships (e.g., India's generic pembrolizumab).
b) Global funds (e.g., UNITAID) for subsidized distribution.
2. Biomarker Expansion:
a) Mobile labs for rural MSI-H/dMMR testing; AI-assisted pathology.
b) WHO-led standardization of biomarker testing protocols.
3. Toxicity & Resistance:
a) Clinician training via tele-mentorship (e.g., Project ECHO).
b) Develop next-gen therapies (e.g., bispecific antibodies, *KRAS* inhibitors).
4. Combination Strategies:
a) Adaptive trials (e.g., platform trials for immunotherapy + targeted therapy).
b) Guidelines for sequencing (e.g., *EGFR* inhibitors before immunotherapy in NSCLC).
5. Policy Advocacy:
a) Mandate insurance coverage for biomarker testing.
b) Fast-track approvals for biomarker-driven therapies.

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Objective of your solution:
(Briefly define the primary outcome of your solution to this challenge):
Targeted solutions, immunotherapies and targeted therapies can be integrated more effectively into clinical practice, providing patients with more personalized and potentially life-saving options by implementing the below written solutions.

Describe your solution / proposal:
Provide a detailed account of your solution/ proposal to this challenge. You could type your

solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):

Immunotherapies and targeted therapies have transformed cancer treatment, offering new hope, but integrating them effectively into existing protocols presents challenges. Immunotherapies, like checkpoint inhibitors, harness the immune system to fight cancer. They've shown effectiveness in cancers such as melanoma, lung cancer, and kidney cancer. The main advantage is the potential for long-lasting responses, even in advanced stages, and generally fewer side effects compared to chemotherapy. However, they're not suitable for all patients, and immune-related side effects (like lung inflammation) can be serious. Targeted therapies, such as tyrosine kinase inhibitors and monoclonal antibodies, target specific cancer mutations. They're highly effective in cancers like chronic myeloid leukemia (CML) and HER2-positive breast cancer. These therapies are precise, leading to fewer side effects. Yet, resistance can develop over time, and access is limited by cost, especially in low-resource settings. Biomarkers are crucial for deciding which therapy to use. For instance, PD-L1 expression helps identify patients who will benefit from immunotherapy, while *EGFR* mutations guide the use of targeted therapies in lung cancer. The main challenges in using these therapies include high costs, limited access to biomarker testing, and the development of resistance. Not all patients respond, and some suffer from significant side effects. To address these, cost reduction through partnerships, wider access to testing, and combination therapies can help overcome resistance. Improving clinician education and ensuring better insurance coverage will also improve access, making these life-saving treatments more available to those who need them most.

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State:
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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):

To decode the art and science of precision: This proposal aims to chart a transformative path for seamlessly integrating emerging immunotherapies and targeted therapies into mainstream oncology protocols, not as adjuncts, but as cornerstones of personalized cancer care.

In an era where cancer biology is no longer a mystery but a map, the objective is to explore how these powerful modalities, each with its own promise and complexity, can be harmonized to create tailored, dynamic treatment blueprints for every patient. By dissecting their clinical efficacy, therapeutic advantages, and translational challenges, we seek to unveil a new therapeutic language where biomarkers guide decisions, not just predictions, and biology drives treatment, not just tradition.

This proposal also dives into the disparities and dilemmas that prevent universal access and applicability be it biomarker variability, immune resistance, or logistical constraints and envisions solutions rooted in innovation, accessibility, and adaptive protocol design.

Ultimately, the objective is simple, yet profound:

To turn precision into practice, and potential into cure.

Because in the future of oncology, personalization isn't the luxury of a few, it's the standard for all.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):

To truly integrate immunotherapies and targeted therapies into routine oncology care, we must bridge precision science with pragmatic clinical strategy. This requires a four-tiered approach: understand, identify, personalize, and democratize.

1. Understand Efficacy & Limitations:
Immunotherapies offer long-term remissions, while targeted therapies deliver rapid, tumor-specific responses. Yet, immune-related adverse events, resistance mutations, and high costs remain barriers. An evidence-based, tumor-type specific approach must guide when and how to combine or sequence these modalities.

2. Biomarker-Driven Protocols:
Biomarkers like PD-L1 expression, MSI status, *EGFR, ALK,* and *BRAF* mutations are the compass for therapy decisions. Incorporating next-generation sequencing (NGS) as a frontline diagnostic tool ensures patients are not just treated but matched to their most effective therapy.
3. Personalized Pathways in Practice:
Multi-disciplinary tumor boards should evolve into Precision Oncology Boards, where oncologists, pathologists, geneticists, and data scientists co-develop treatment plans. Adaptive algorithms can help modify protocols in real-time based on response and resistance patterns.
4. Addressing Access and Equity:
Solutions must tackle cost and infrastructure. Biosimilars, value-based pricing, public-private funding, and diagnostic subsidies can make advanced therapies accessible. Global frameworks like WHO's essential medicines lists should evolve to include critical immunotherapies and targeted agents.
This integration is not merely clinical, it's conceptual.
It is the shift from 'one-size-fits-all' to 'biology-tailored blueprints', where science respects individuality and systems support access.
The future of oncology is not just targeted. It's tailored, tested, and truly transformative.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To significantly improve patient survival rates and quality of life through the global implementation of personalized, AI-driven cancer treatment, minimizing toxicities and maximizing the effectiveness of immunotherapies and targeted therapies.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Effectiveness & Challenges of Emerging Therapies
1. Immunotherapy (PD-1/CTLA-4, CAR-T)-Durable responses, "immune memory", but also Hyperprogression (20%), irAEs (colitis, pneumonitis)
2. Targeted Therapy (*PARP*, TKIs) - High tumor specificity, less systemic toxicity, but also resistance (e.g., *EGFR* T790M), narrow biomarker-defined populations.
Key Biomarkers for Decision-Making
1. Immunotherapy: PD-L1 (>1%), TMB (>10 mut/Mb), MSI-H/dMMR
2. Targeted Therapy: *EGFR/ALK* (lung), *BRCA* (ovary), *NTRK* (pan-cancer)
3. Novel AI Biomarkers: Radiomics (CT texture predicts IO response), ctDNA dynamics.
Critical Challenges in Utilization
1. Cost: 80% of Indians ineligible
2. Infrastructure: Lack of NGS, cryopreservation for CAR-T

3. Toxicity Management: Rural areas lack specialists for irAEs
4. Trial Gaps: Underrepresentation of Indian genomic diversity lack of predictive markers for many cancers.

- First, develop a global, AI-powered platform integrating patient data (genomics, imaging, clinical history), real-time monitoring, and a comprehensive database of clinical trials and treatment outcomes. AI would predict individual responses to treatment combinations, personalize therapy, and adjust in real-time based on biomarker changes and adverse events. Dynamic Protocol Engine: AI combines IO + targeted therapy based on real-time biomarkers (e.g., start with osimertinib for *EGFR*+ NSCLC, switch to IO if T790M- ctDNA emerges).
- Second, create standardized, cost-effective manufacturing processes and novel reimbursement models to improve accessibility, like Modular GMP labs in district hospitals.
- Third, establish comprehensive training programs for healthcare professionals in the use and management of these therapies.
- Finally, invest heavily in biomarker discovery and validation. For e.g., use hospitals pool anonymized NGS data → train AI to discover India-specific biomarkers.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Enhanced clinical outcomes through the personalized integration of immunotherapy and targeted therapies—resulting in improved survival, reduced treatment-related toxicity, and increased access to precision oncology, especially in diverse and resource-limited settings.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Integrating emerging immunotherapies and targeted therapies into existing cancer treatment protocols is essential to improving patient outcomes. These approaches offer precision-based treatment by leveraging tumor biology and host immune modulation, resulting in improved survival and quality of life. Effectiveness and Challenges Checkpoint inhibitors and targeted therapies (e.g., *EGFR, ALK*, *BRAF* inhibitors) have transformed care in several malignancies such as NSCLC, melanoma, and RCC. However, challenges include immune-related adverse events, primary or acquired resistance, high treatment costs, and limited real-world data outside clinical trials.
1. Biomarkers in Decision-Making: Biomarkers like PD-L1 expression, tumor mutational burden (TMB), MSI-H/dMMR status, and oncogenic driver mutations guide therapy selection. Integrating liquid biopsy and NGS panels enhances timely and accurate decision-making.
2. Utilization Barriers: Barriers include limited access to molecular diagnostics, high cost of drugs, clinician unfamiliarity in low-resource settings, and disparities in reimbursement and regulatory pathways.
3. Proposed Solutions:

- Develop national and institutional treatment algorithms combining traditional and novel therapies.
- Strengthen molecular testing infrastructure and ensure equitable access.
- Promote clinician education and multidisciplinary tumor boards for optimized decision-making.

- Support local clinical research, including trials on low-dose immunotherapy, cost-effective regimens, and novel combinations.
- Encourage policy frameworks and public-private partnerships to facilitate affordable access and faster regulatory approvals.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Immunotherapies and targetted therapies must be considered in patients if indicated. Certain biomarkers for testing must be employed so that these therapies may be channelled only to those for whom it is indicated. The government must take measures to bring these therapies in at least one Govt institution in each state so that it can be utilized by many patients.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
The advent of immunotherapies & targeted therapies has paved for a better improvement in therapeutic options by increasing survival and providing a better quality of life for the patients. But can it be available to every patient in our country? That is the question.
Because of their mechanism of specifically targeting the cancer cells, the side effect burden is comparatively less when compared to cytotoxic chemotherapy. But in a country like India, where finances play a major role it is important for us to choose the right patient, the therapy. Not only this, the other problem that we face, is the need for a good supportive care centre to the manage the toxicities related to Immunotherapies. But IO cannot be given in every patient with cancer. It must be utilized judiciously in those patients, in which its benefits outweigh the risks. So, a reliable biomarker is needed to channel patients who can receive IO or targeted therapies. In case of IOs, PDL1 testing, Tumor mutational burden, TILs, TPS/CPS scores can play a important role in deciding treatment. In case of targeted therapies, specific targets should be tested.
For these therapies to be available for most of the patients we may need to:
1. Test for biomarkers which helps in selecting the patient population
2. Consider Low dose IO agents in resourceless settings
3. Provisions to be made by the Govt to make it available in lesser cost in at least one Govt cancer care centre in each state
4. To set up good oncopathological laboratories for testing biomarkers
5. Well trained expertise.

By doing these, I think we can help these therapies to reach many needy people in our country.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Immunotherapy prognostication markers, challenges in Indian patients and steps to overcome them.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Immunotherapy, like nivolumab, offers significant advantages in resource-limited settings like India, achieving durable remission in 20-40% of lung or head-neck cancer patients, outlasting chemotherapy. Its manageable toxicity (e.g., less myelosuppression) enhances quality of life, and outpatient delivery reduces hospital costs.
Fewer cycles (e.g., pembrolizumab every 3-6 weeks) suit patients with limited access. However, costs (1-4 lakh/dose) burden 60% out-of-pocket payers. Scarce infrastructure (1,500 oncologists nationwide) and expertise to manage immune-related adverse events (irAEs), like colitis, limit rural reach.
Low awareness and biomarker testing delays optimal use.

Biomarkers in Therapy Selection
1. Predictive biomarkers identify immunotherapy responders. PD-L1 expression (≥50%) predicts pembrolizumab success in NSCLC (45% response rate), while MSI-H status flags colorectal cancer responders (40-50%).
2. Prognostic biomarkers, like high TMB (>10 mutations/Mb), suggest better nivolumab outcomes in NSCLC. *BRCA* mutations guide breast cancer therapy with immunotherapy potential. In India, NGS testing (50,000-1 lakh) is scarce, with PD-L1 testing in <20% of centers, risking inefficient therapy. Subsidized diagnostics and pathologist training can ensure precise, cost-effective treatment.

Challenges and Solutions in India
1. Immunotherapy faces high costs, limited access (1 oncologist per 900,000), and irAE management gaps in 70% of hospitals.
2. Low biomarker adoption and biosimilar delays exacerbate issues.
3. Solutions include scaling biosimilars to cut costs by 30-40%, expanding Ayushman Bharat subsidies for drugs and NGS, and building regional hubs with telemedicine.
4. Training 5,000+ oncologists via CMEs, leveraging ICMR data for guidelines, and using community workers to boost awareness can help.
5. Faster DCGI biosimilar approvals (20-30% cost reduction) and tumor boards for biomarker-driven decisions will optimize immunotherapy for India's 1.5 lakh cancer patients.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Title: Integrating Immunotherapy in Acute Myeloid Leukemia (AML)
Background: Patients with Acute Myeloid Leukemia (AML), particularly those classified under the French-American-British (FAB) subtypes M4 and M5, often present with lymphadenopathy and

extramedullary disease. These subtypes generally have poorer outcomes compared to other AML variants, potentially due to the involvement of a lymphoid component.
Rationale: We aim to explore the therapeutic potential of targeting the lymphoid component in AML M4/M5 using immunotherapy. By integrating PD-L1 inhibition into standard treatment regimens, we hypothesize that outcomes in this subset of patients can be improved.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Study Design Overview
1. Patients diagnosed with AML M4/M5 who are planned for treatment with Azacitidine plus Venetoclax and who present with lymph node or extramedullary involvement will be enrolled. These patients will undergo PD-L1 expression assessment.
2. Treatment Protocol: In addition to Azacitidine and Venetoclax, patients will receive a PD-L1 inhibitor (e.g., Atezolizumab).
3. Scientific Basis
Venetoclax, a BCL-2 inhibitor, can induce immunogenic cell death (ICD). This process leads to the release of damage-associated molecular patterns (DAMPs), thereby enhancing tumor immunogenicity and making immunotherapeutic strategies, such as PD-L1 inhibition, more effective.
4. Endpoints
- Overall Response Rate (ORR)
- Progression-Free Survival (PFS)
- Overall Survival (OS)

4. Stratification
Patients will be stratified based on PD-L1 expression levels into three groups:
- <1%
- 1%-10%
- >10%

This stratification will help determine whether the degree of PD-L1 expression correlates with response to combined immunotherapy and standard AML treatment

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To effectively integrate emerging immunotherapies and targeted therapies into existing treatment protocols to improve patient outcomes

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Effectiveness and advantage of immunotherapy:
1.Only curative option in renal cell carcinoma, relapsed Hodgkin's lymphoma, melanoma

2.Highly effective with best 5-year survival rates in metastatic melanoma, metastatic RCC, MSI high metastatic GI malignancies
3.Sustained efficacy, prolonged disease response in all malignancies due to immune memory
4.100 percent disease control in non-metastatic MSI high colorectal cancer

Effectiveness and advantages of targeted therapy:

1.Easy to administer, mostly oral drugs
2.Lesser adverse events compared to chemotherapy
3.Treatment can be tailored according to cancer genomics of each patient, increasing the response rates, survival and also reducing the toxicity

Biomarkers for immunotherapy:

1.PDL1 levels
2.MSI / dMMR status
3.TMB
4.Immunoscore
5.Under research (soluble PDL1, TCR clonality, gut microbiome, ctDNA, immunophenotyping)

Biomarkers for targeted therapy:

EGFR - Osimertinib
ALK - Alectinib, Lorlatinib
ROS - Entrectinib
Her2 - Pertuzumab, trastuzumab

Challenges in utilization of targeted therapy and immunotherapy and its solutions:

1.Diagnostic assays for biomarker testing - Developing cheaper assays like IHC and Fish /PCR so it can be done in all Indian cancer centres eg: dMMR, p53, Her2 testing by IHC had made it readily available in all centers
2.High cost of therapy - Understanding the pharmacokinetics and pharmacodynamics of the drugs and modifying the dose and regimen to make it more affordable for Indians eg. Low dose nivolumab in head and neck, cervical cancer and Hodgkin's lymphoma.
3.Dependence on imports and lack of innovation - R&D investment by indigenous pharma companies, as well as academic cancer centres and ICMR to develop 'desi' immunotherapy and targeted therapy eg. anlotinib and tislelizumab by China has
saved money for them
4.Limited Indian data - Most of our therapy is based on western data. The genomics and physiology of Indians are entirely different from westerners. We need our own cohort data so that we can better understand the efficacy and toxicity profile of these patients and modify the dose of drugs and regimen based on these data
5.Regulatory barriers - Govt should make important drugs like trastuzumab, nivolumab, osimertinib and lorlatinib under Ayushman Bharath scheme, so that it is available at subsidized rates for all Indians

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To find better biomarker that predicts response.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):

1) Effective combinations of IO, targeted therapy with chemotherapy includes
A- Osimertinib + Pemetrexed-Carboplatin in *EGFR* exon 18,21 mutation NSCLC
B- Pembrolizumab + Pemetrexed-Cisplatin in NACT in NSCLC (Non squamous)
C- Nivolumab with Gemcitabine and Cisplatin in NACT in Urothelial cancer
D- Enfortumab Vedotin + Pembrolizumab in metastatic Urothelial ca
E- Pembrolizumab + Paclitaxel-Carboplatin in NACT TNBC.
Advantage: Increased PFS & OS

Challenges:
a) Cost of drug, b) increased adverse effects c) Management of toxicity. d) Convincing benefit of immunotherapy/ targeted therapy in adjuvant setting
2) Biomarkers:
A) PD-L1
B) TMB
C) HRD in ca ovary, ca prostate
D) *RAS* in ca colon
E) *EGFR* mutation in exon 19, 21

3)
A) Biggest hurdle is cost though it is not an issue for all patients, like adjuvant setting where IO is required for specific duration. But in metastatic setting, to convince to continue till progression of disease is difficult. So, studies must come for treatment gaps.
B) Lack of concordance between PD-L1 score and response.
C) Toxicity that precludes IO use such as myocarditis, demyelination polyneuropathy.

4)
A) Low dose IO, (Minimum target concentration) for eg, Amivanatmab 350 mg is minimum effective dose achieving response.
B) To start with desensitization protocol for all IO/Targeted agents.
C) More flexible PAP in metastatic setting
D) Loan from pharma company offering with no interest, it's investment
E) To share spreadsheets of toxicity with managing toxicity with prescribing Oncologist
F) To increase DCGI approvals

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Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
Integrating Emerging Immunotherapies & Targeted Therapies to Improve Patient Outcomes

In today's era of precision oncology, immunotherapies and targeted therapies have become powerful tools in our fight against cancer. But their true impact is realized only when they are thoughtfully integrated into existing treatment protocols, ensuring that every patient benefits from the best science has to offer.

Effectiveness, Strengths, and Challenges in the Clinic

1. Why these therapies matter:

Immunotherapy, such as checkpoint inhibitors (e.g., nivolumab, pembrolizumab), has revolutionized outcomes in diseases like lung cancer, melanoma, and Hodgkin lymphoma. In some patients, it leads to long-lasting remission.

Targeted therapies, like EGFR inhibitors in NSCLC or PARP inhibitors in BRCA+ cancers, offer precise and often oral treatments, tailored to a tumor's genetic profile.

2. Advantages:

Benefit

- Precision: Targets cancer-specific mutations or immune pathways
- Personalized: Based on patient's biomarker or tumor profile
- Better Tolerability: Often fewer systemic side effects compared to chemo
- Durable Outcomes: Especially in immunotherapy-responsive cancers
- Quality of Life: Many oral or less toxic regimens preserve daily living

3. Challenges:

Issue

- Resistance: Tumors can become resistant over time (especially in targeted therapy)
- Autoimmune Toxicity: Immune-related adverse effects (e.g., colitis, thyroiditis) can be
- life-threatening
- Cost: These treatments are often extremely expensive and may not be reimbursed
- Access to Testing: Molecular and biomarker testing isn't always available or timely
- Not Universal: Some patients simply don't respond even with the right markers

Biomarkers That Guide Treatment Decisions

To deliver personalized cancer therapy, biomarkers guide us in matching the right patient to the right treatment.

Biomarker Guides, Use of Cancer, Type

- PD-L1 Expression Immunotherapy (PD-1/PD-L1 inhibitors) Lung, HNSCC, bladder, TNBC
- MSI-H/dMMR, Immunotherapy (e.g., dostarlimab) Colorectal, endometrial, gastric
- EGFR mutation, EGFR inhibitors (e.g., osimertinib), NSCLC
- ALK, ROS1, RET fusions ALK/ROS1 TKIs (e.g., crizotinib) NSCLC
- HER2 amplification HER2-targeted therapy (trastuzumab, Enhertu) Breast, gastric, NSCLC
- BRCA1/2 mutation (HRD) PARP inhibitors (e.g., olaparib) Breast, ovarian, pancreatic
- NTRK fusion TRK inhibitors (e.g., larotrectinib), Any solid tumor with fusion
- TMB-H (Tumor Mutational Burden) Broader eligibility for immunotherapy Multiple cancers

Bottom line: Biomarkers are the 'roadmap' for integrating modern therapies.

Challenges in Utilizing These Therapies for All Patients

Despite their promise, many real-world barriers make widespread use difficult:

1. Clinical & Operational Challenges

- Limited testing infrastructure (especially in smaller centers or low-income countries)
- Delays in getting NGS or IHC reports
- Uncertainty about which patients will truly benefit
- Economic Challenges
- High out-of-pocket costs or lack of insurance coverage

- Inconsistent reimbursement policies across hospitals and regions

2. Knowledge & Training Gaps
- Some clinicians may not be fully trained in molecular oncology
- Lack of awareness about available biomarkers or how to interpret them

3. Equity Challenges
- Urban-rural divide: rural patients often have no access to molecular testing
- Global disparity: high-income countries access latest therapies, while LMICs lag behind

4. Practical Solutions to Improve Integration

There are ways to overcome these barriers. some already working well in practice.

Solution: How It Helps
- Molecular Tumor Boards: Help clinicians make personalized decisions using expert input
- Centralized Testing Hubs: Shared NGS/IHC labs can serve multiple smaller hospitals
- Tiered Pricing & PAPs: Pharma can offer discounts or free therapy for eligible patients
- Digital Platforms: Help track biomarkers, access trials, or enroll in assistance programs
- Oncology CME Programs: Continuous education for oncologists to stay current
- Advocacy & Policy Push: Add immunotherapy and testing to national insurance schemes or EML lists
- Real-World Data Registries: Capture Indian/LMIC-specific outcomes to drive guidelines and funding

Ultimately, equity and innovation must go hand-in-hand.

Final Word: The integration of immunotherapy and targeted therapy isn't just about science, it's about people. It's about a woman with lung cancer in a rural town getting a test in time. A man with melanoma living years longer because someone added immunotherapy to his plan.

If we can blend modern innovation with access, training, and compassion, we can ensure that these game-changing treatments reach the patients who need them most, not just in theory, but in practice.

Full Name:
Viji V Julian

Name of the Institution:
Madras Medical College

State:
Tamil Nadu

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To overcome the challenges in combining immunotherapy with targeted therapy.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):

Targeted therapies induce rapid tumor regressions with a consequent decrease in tumor associated immunosuppression, tumor senescence and facilitating immune clearance by T cells. Immunotherapy consolidates the effect of targeted chemotherapy due to its synergy into prolonged durable remissions.

Eg

1. Epigenetic therapies plus immunotherapy - to overcome ICB resistance (Etinostat, Azacytidine)
2. MAPK inhibitors with immunotherapy- Inhibits mutant BRAF, associated with immune escape and an immunosuppressive TME (Dabrafenib+trametinib, Cobimetinib)
3. VEGF inhibitors with immunotherapy (Bevacizumab, sunitinib, axitinib)

Biomarkers: Tumor microenvironment - cytokines, tumor mutation burden, TILs Tumor related - PDL1, TMB, MSI Immunotherapy resistance markers - KRAS, STK11, KEAP1

Challenges- dosing, timing, sequencing and adverse effects Adequate dosing and side effects are detected with clinical trials Concurrent use of targeted therapy and immunotherapy simultaneously promotes a favorable microenvironment along with T cell activation for durable prolonged synergistic effects rather than sequencing.

Full Name:
Aishwarya Ghule

Name of the Institution:
Deenanath Mangeshkar Hospital

State:
Maharashtra

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Better integration of immunotherapy and targeted therapies in routine protocols.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
To provide awareness for PD L1, MSS testing and TMB testing by educating about the latest approvals for its integration in Neoadjuvant, adjuvant and palliative settings. Provide one free test PDL 1 or MSS for approved indication for the lower income people and those who guarantee to use the immunotherapy further.

Full Name:
Pankaj Deep Rana

Name of the Institution:
Metro Hospital and Cancer Institute

State:
Delhi

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Integration of immunotherapies and targeted therapies into standard cancer protocols has the potential to significantly improve outcomes when guided by biomarker-driven approaches. However, successful implementation requires overcoming barriers related to cost, testing access, and infrastructure. A multi-stakeholder effort involving clinicians, policymakers, industry, and patient advocates is essential to ensure equitable access and optimal use of these innovations in oncology.

Describe your solution / proposal: Provide a detailed account of your solution/ proposal to this challenge. You could type your solution/ proposal here. (Disclaimer: Solution/proposal should not exceed more than 300 words.):
1. Effectiveness, Advantages, and Clinical Challenges
A. Immunotherapies (e.g., Checkpoint Inhibitors, CAR-T Cells)
Effectiveness:

- Durable responses in certain cancers (e.g., melanoma, NSCLC, RCC, Hodgkin's lymphoma).
- Induces immune memory for long-term cancer control.

Advantages:

- Lower risk of resistance compared to chemotherapy.
- Long-lasting effects in responders.
- Can be combined with other treatments for synergy.

Challenges:

- Benefit limited to a subset of patients.
- Immune-related adverse events (irAEs) can be serious.
- Expensive and logistically demanding (e.g., CAR-T cell therapy).

B. Targeted Therapies (e.g., *EGFR, ALK, BRAF* Inhibitors)

Effectiveness:

- High response rates in molecularly defined subgroups.
- Predictable pharmacodynamics and side-effect profiles.

Advantages:

- Precision-based approach, fewer off-target effects.
- Oral availability in many agents enhances compliance.

Challenges:

- Development of resistance over time (e.g., T790M mutation in *EGFR*).
- Limited efficacy in absence of specific mutations.

2. Biomarkers for Therapy Decision-Making

Therapy, Predictive Biomarkers, Cancer Types

- Immunotherapy PD-L1 expression, MSI-H/dMMR, TMB-high NSCLC, melanoma, colorectal, bladder
- EGFR inhibitors, EGFR mutations, NSCLC
- ALK inhibitors, ALK rearrangement, NSCLC
- BRAF inhibitors, BRAF V600E mutation, Melanoma, colorectal

3. Challenges in Universal Utilization

1. Biomarker Testing Barriers:

- Limited access in resource-poor settings.
- Turnaround time delays treatment initiation.
- Reimbursement issues for next-gen sequencing.

2. Cost and Accessibility:

- High cost of therapy (e.g., CAR-T therapy, checkpoint inhibitors).
- Limited insurance coverage or government support.
- Inadequate infrastructure for storage and delivery.

3. Patient Selection & Resistance:

- Lack of reliable predictive biomarkers in some cases.
- Acquired resistance mechanisms (e.g., secondary mutations).
- Heterogeneous tumor biology leading to treatment failure.

4. Solutions to Improve Integration

A. Enhancing Biomarker Access and Interpretation:

- Expand access to molecular diagnostics (e.g., liquid biopsy, NGS panels).
- Develop rapid, low-cost testing platforms.
- Train pathologists and oncologists in genomic literacy.

B. Cost-Containment Strategies:

- Negotiate pricing through value-based reimbursement models.
- Promote use of biosimilars and generics.
- Implement national patient access programs (e.g., similar to GIPAP for CML).

C. Clinical Decision Support:

- Integrate AI-driven clinical decision tools in EHRs.
- Establish multidisciplinary tumor boards with molecular pathologists.
- Use real-world data registries to guide local protocols.