Title:
Impact of steroids on cancer immunotherapy

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Since steroids can alter the immune response and perhaps compromise the efficacy of immunotherapeutic therapies, they can have a big impact on cancer immunotherapy. Steroid use in cancer patients undergoing immunotherapy is a complicated matter, and the effects might differ based on a number of variables, such as the immunotherapy type, the patient's circumstances, and the timing of steroid delivery.

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) As important as human life is, steroids such as dexamethasone and prednisone are necessary for cancer treatments because they decrease the side effects, decrease inflammation and manage the symptoms.
Besides the amount of medicine and the time it is taken, the other two factors, "Total Treatment Time" and "Total Biological Effectiveness" are of equal importance in ensuring the minimum side effects in therapies.
However, before reaching that point, people should be aware of the applicable roles and relevant steps. Taking chemotherapy very time is quite tough that is only a few are able to tolerate.
More than ever, the presence of such inhibitors has made the study of cancer and its treatment very easy.
1. Pre-treatment (before immunotherapy, chemotherapy, or radiation)
Objectives: To provide corrections that decrease the discomfort of having chemotherapy (CINV) Auxiliary means such as before and while chemotherapy (e.g. doxorubicin or dexamethasone with cisplatin). Irregular responses from infusions, for instance, a drip Before starting the monoclonal antibody targeting therapy (for example, rituximab, pembrolizumab). For edema and inflammation control and also is utilized to reduce the swelling of the brain tumor (dexamethasone before radiation). Timing: Preventing AEs is usually done on 30-60 min prior to the therapy. The DA is given 1-2 days before the emetogenic treatment in severe cases-Taube (2015) p.38-16 by Taube, (2015).
2. Throughout Therapy (Concurrent with Treatment) Target: Inflammatory reactions in patients after immunotherapy and radiotherapy are the main issue. IRAEs and CIPBK are not bothered by the use of immune checkpoint inhibitors. To minimize hypersensitivity reactions, the use of tyrosine kinase inhibitors and some other targeted therapies is recommended. Timing: The medicine is provided once a day following the severity of the rating of the patient's side effects or as necessary. Tapering of steroids is mandatory in some people who receive chemotherapy for a very long period to avoid deleterious effects of withdrawal.
3. After Therapy Completion (Post-Treatment) Goal: The primary objective is to reduce the delayed chemotherapy side effects such as the immune system's ever-radiation induced edema. On the other hand, it can be used to heal the severe consequences of immunotherapy among other things. Timing: The therapy is applied for a short time, 3-5 days, for prompt cure of the acute effects of the treatment.

If it is needed for a long time to prevent adrenal insufficiency, they should be tapered through a few weeks.
Some good thoughts to keep in mind:
Dose down and Taper: Withdrawal should not be done suddenly to prevent the risk of adrenal gland suppression.
The Personal Factors: Consider metabolic disorders such as osteoporosis and diabetes mellitus.
Follow-up: Observe the patient for any possible adverse effects like immunosuppression, muscular atrophy, or hyperglycemia.

B)
Approaches to Balance Steroid Benefits & Immunotherapy Efficacy-
Steroids are vital in countering the side effects of cancer therapies, but too much of their use can lead to immune suppression, thus reducing the effectiveness of immunotherapy. The task is to treat the side effects of cancer carefully without damaging the effect of anti-cancer immunity.
1. Use Steroids Only When Absolutely Necessary Risk-Based Approach:
Mild immune-related adverse events (irAEs): Instead of using steroids first-line, they should be treated with supportive therapy as NSAIDs, antihistamines.
Administer low-dose, short-duration steroids (e.g., 10 mg per day) to alleviate mild symptoms.
Severe side effects: If you have adverse effects, physicians may increase the dosage while following a systematic tapering schedule.
Stepwise Escalation: Before you apply systemic steroids, you can first initiate usage of topical or inhaled steroids for minor issues (topical hydrocortisone, the skin damage will be reversible, budesonide using colitis, etc.).
Treat with the lowest dose for the shortest period if systemic steroids are necessary.
2. Optimize Timing & Dosing Strategies Delay Steroid Introduction:

- Before deciding on steroid therapy, if possible, let immunotherapy first work a bit and then the immune system will be stronger.
- As an instance, by postponing the use of steroids for two to four weeks after the checkpoint inhibitors are introduced, longer T-cell priming can be achieved.
- Taper Steroids Carefully: Do not subscribe to prolonged high-dose steroid use in order to avoid immune system suppression. Along with the process of de-immunological suppression, it is essential to reduce the rate of de-tapering of prednisone over 4-6 weeks.

3. Explore Alternative Immunosuppressants Employ Steroid-Sparing Substances: Here are the immunosuppressants that do not influence T-cell activation but may cure severe complications like colitis.
One of these dates will be in the selection of TNF-ϒ inhibitors for colitis, e.g., infliximab.
The next step is the use of IL-6 inhibitors for toxicities induced due to cytokine, in this case, for example, tocilizumab.
The last line of defense would be inhibitors of calcineurin or mycophenolate mofetil for steroid-refractory conditions. Personalized Immunosuppression:
To determine if the patient should receive steroids or other treatments, consider factors such as patient biomarkers, for instance, immune cell profiles and cytokine levels.
4. Close Monitoring & Biomarker-Guided Adjustments Track Immunological Response While Using Steroids: In order to assess the immunological responses, peripheral blood T-cell activity, PD-L1 expression, and cytokine levels should be done to the patients taken the drug. It may be safer to put steroids off quicker if the immunological response is still strong. Regular Imaging and Response Monitoring: In PET-CT or MRI scans, it will be determined if steroids are affecting the response to immunotherapy by following up alterations in tumor size and immune cells.

C)
Develop solutions on individualizing steroid administration in cancer care.
Strategies for Tailored Steroid Administration in Cancer Treatment-

To characterize, the use of steroids in lung cancer treatment requires flexibility to avoid drug adverse reactions and to obtain therapeutic effects.
The use of the drug must be tuned, minimizing the toxic effects and immune suppression and enhancing the therapeutic results.
This equilibrium can be retrieved with the use of an adjusted strategy guided by patient's variables.
1. Risk Assessment by Patient Group of Patients According to Risk

- Patients at low risk: Steroid use should be avoided or reduced (supportive care alternatives).
- For individuals at moderate risk, use low-dose, short-course steroids under careful observation.
- High-risk patients: Increase dosages but taper them quickly and keep an eye on their immune systems. > Look into the patient's comorbidities.

Diabetes: Use non-steroidal anti-inflammatory ways to keep hyperglycemia at bay.
Cardiovascular disease: Strictly use steroids on patients that do not encounter hypertension.
Osteoporosis: Include bone-protective drugs and consider the decrease of long-term steroid usage.
2. Precision-Based Steroid Dosing & Timing Use of Biomarkers and by Clubs of Therapy

- Safe and Effective Mixes The study of hormones like thyroid-stimulating hormone, FSH, estradiol, and prolactin helps in identifying the existence of endocrine dysfunction.
- Utilize Biomarkers for Direct Treatment
  TNF-ϒ±, IL-6, and CRP are inflammatory indicators that can be used to predict who needs steroids and who doesn't.
  To analyze the tumor microenvironment that will help in the identification of the danger of immune suppression resulting from steroids.

Methods Without Using Steroids
Local administration: Rather than systemic steroids, use topical, inhalation, or intra-articular steroids.
Immunosuppressants that Spare Steroids: When feasible, use JAK inhibitors, TNF- ϒ ± blockers (infliximab), or IL-6 inhibitors (tocilizumab).
Dynamic Modifications to - Go slowly and start low:
Start with the lowest dose that works best and only raise it if required.
Taper depending on response: To ascertain when steroids can be safely taken down, use biomarker and symptom surveillance.
3. Real-Time Monitoring & AI-Based Predictive Models Customized Steroid Usage using AI and Digital Instruments

- AI-powered risk prediction algorithms can recommend the best dosages and assist in determining who actually needs steroids.
- Steroid metabolism, patient reactions, and side effects may all be tracked in real time by intelligent algorithms.
- Wearable technology and remote observation: In patients receiving steroid treatment, use equipment to monitor blood pressure, glucose levels, and inflammation markers. Adapt dosages dynamically based on individual patient reactions.

4. Integration into Multidisciplinary Cancer Care Multidisciplinary Steroid Stewardship Team
Immunologists, oncologists, and endocrinologists work together to create customized steroid regimens.
Patient Education and Shared Decision-Making: Help patients balance the advantages and disadvantages of steroid treatment.
Teach patients self-monitoring skills and steroid side effects using digital health apps.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Primary Outcome of the Solution:
1. Preserved Immunotherapy Efficacy: Minimized steroid interference with immune activation by restricting use to severe immune-related adverse events (irAEs) and avoiding prophylactic/preemptive administration.
2. Effective irAE Management: Timely, dose-optimized steroids for Grade 3–4 toxicities (e.g., pneumonitis, colitis) to prevent morbidity/mortality without compromising antitumor responses.
3. Personalized Treatment: Steroid use tailored to tumor biology (e.g., TMB status), patient biomarkers (e.g., lymphocyte counts), and comorbidities to maximize benefit-risk balance.

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.):
Impact of Steroids on Cancer Immunotherapy
1. Optimal Timing of Steroid Administration
• Pre-Immunotherapy:
a) Avoid prophylactic steroids unless critical (e.g., brain metastases with edema), as they may blunt immune activation.
• During Immunotherapy:
a) Delay steroids for mild immune-related adverse events (irAEs; e.g., Grade 1–2 rash) to preserve efficacy.
b) Reserve high-dose steroids (e.g., ≥1 mg/kg prednisone) for severe irAEs (Grade 3–4 colitis, pneumonitis).
• Post-Immunotherapy:
a) Taper steroids rapidly once irAEs resolve to minimize prolonged immunosuppression.

2. Balancing Benefits (Side Effect Management) vs. Risks (Reduced Efficacy)
• Dose Minimization: Use the lowest effective steroid dose (e.g., 0.5 mg/kg prednisone for hepatitis).
• Alternative Agents:
a) For mild-moderate irAEs: Topical steroids (rash) or non-immunosuppressive therapies (e.g., vedolizumab for colitis).
b) For endocrine irAEs: Hormone replacement (e.g., levothyroxine) over steroids.

• Selective Timing: Administer steroids after immune checkpoint activation (e.g., post-first cycle) to reduce interference.

3. Individualizing Steroid Administration

• Tumor-Specific Factors:

a) Steroids may be less detrimental in hypermutated tumors (e.g., melanoma) with robust immune infiltration.

b) Avoid low TMB cancers (e.g., pancreatic) where immunotherapy efficacy is already limited.

• Patient-Specific Factors:

a) Biomarkers: High baseline lymphocyte counts may predict better tolerance to steroid interruption.

b) Comorbidities: Prioritize steroids in frail patients at risk of irAE complications.

• Monitoring Tools:

a) Serial immune profiling (e.g., CD8+ T-cell counts) to guide steroid tapering.

b) Liquid biopsies (ctDNA) to detect early tumor progression during steroid use.

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Objective of your solution:
(Briefly define the primary outcome of your solution to this challenge):
Incorporating steroids into the care of cancer patients undergoing immunotherapy requires a careful, individualized approach. By balancing the need to manage side effects with the goal of maximizing immunotherapy efficacy, healthcare providers can help enhance patient outcomes while minimizing potential risks. Tailoring steroid administration to each patient's needs, minimizing their use, and opting for alternatives where possible will optimize the effectiveness of cancer immunotherapies.

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.):
Steroids are often used in cancer care to manage inflammation, pain, and side effects from treatments like chemotherapy and immunotherapy. However, their use in combination with immunotherapy requires caution because steroids can suppress the immune system, potentially reducing the effectiveness of treatments designed to enhance immune responses, such as checkpoint inhibitors. The timing of steroid administration is crucial. Using steroids before or during immunotherapy can interfere with the immune system's ability to respond to the treatment. However, steroids may be necessary after immunotherapy to manage immune-related side effects, like skin rashes or gastrointestinal issues. Ideally, steroids should be given post-treatment when needed, and at the lowest dose and for the shortest duration possible to avoid impairing the immune response. To balance the benefits of managing side effects with the risk of reducing immunotherapy efficacy, it's important to minimize steroid use. In some cases, doctors can use alternative treatments for side effects, such as immune modulators that don't suppress immune function as much as steroids. Close monitoring of immune-related adverse events allows for early intervention, reducing the need for high-dose steroids. Individualizing steroid use is key. Factors like age, comorbidities, and the type of cancer should be considered when deciding whether to use steroids. Personalizing the approach, with careful monitoring of the patient's immune response, ensures that the benefits of immunotherapy are maximized while still managing side effects effectively.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Steroids can have both positive and negative impacts on immunotherapy: *Balancing benefits and risks*: Clinicians must balance the benefits of steroids for symptom management with the potential negative impacts on immunotherapy efficacy.

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.):
Steroids can have both positive and negative impacts on cancer immunotherapy:
Negative Impacts
1. Immunosuppression: Steroids can suppress the immune system, which may reduce the effectiveness of immunotherapy.
2. T-cell suppression: Steroids can decrease T-cell activity, which is crucial for immunotherapy.
3. Reduced efficacy: Steroids may reduce the efficacy of immunotherapy by suppressing the immune response.
Positive Impacts
1. Symptom management: Steroids can help manage symptoms such as inflammation, edema, and pain in cancer patients.
2. Reducing side effects: Steroids can reduce side effects associated with immunotherapy, such as immune-related adverse events (irAEs).
Clinical Considerations
1. Balancing benefits and risks: Clinicians must balance the benefits of steroids for symptom management with the potential negative impacts on immunotherapy efficacy.
2. Dose and duration: The dose and duration of steroid use can impact the effectiveness of immunotherapy.
3. Monitoring: Close monitoring of patients receiving steroids and immunotherapy is essential to optimize treatment outcome.
Timing when to administer steroids
Two potentially important considerations surrounding steroids and ICI are their dosing and timing. One would intuitively presume that a short course of low-dose steroids administered months following a complete response might result in very different effects from higher doses given the same day of ICI initiation.

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

To illuminate the delicate dance between suppression and stimulation—this proposal seeks to unravel the nuanced interplay between steroid administration and cancer immunotherapy, with the goal of preserving therapeutic potency while protecting patient well-being. As immunotherapy redefines cancer treatment by awakening the body's own defense system, the use of steroids—longstanding allies in symptom control—presents a paradox. They can silence immune overactivity yet may also mute the very signals that drive immunotherapeutic success. This work aspires to explore this therapeutic tightrope with scientific rigor and clinical creativity. The objective is to identify optimal windows for steroid intervention, where inflammation is controlled without compromising immune priming; to construct strategies that balance immune-related toxicity with anti-tumor efficacy; and to ultimately champion personalized steroid protocols, where timing, dosage, and indication are tailored to the biology of both the tumor and the host. By decoding the steroid-immunotherapy interface, this proposal aims to ensure that managing side effects never comes at the cost of compromising the cure. Because in precision oncology, moderation must be masterfully precise.

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.):

Steroid use in cancer immunotherapy must be guided by precision, purpose, and timing to avoid dampening therapeutic efficacy while still managing toxicity.

1. Timing is Critical: Early steroid use, particularly within the first 4 weeks of initiating immune checkpoint inhibitors (ICIs), has been associated with reduced survival outcomes, especially when used for non-immune-related reasons (e.g., symptomatic brain metastases). Thus, steroids should be avoided during immunotherapy initiation unless necessary and delayed until immune activation is established when possible.
2. Balancing Benefits and Risks: Steroids remain the cornerstone for managing immune-related adverse events (irAEs), which, if left unchecked, can be life-threatening. The goal is to use the lowest effective dose for the shortest duration. Tapering schedules should be cautious yet swift, ideally guided by standardized irAE management protocols.
3. Individualized Approach: Patient-specific factors—cancer type, burden of disease, comorbidities, and prior therapies—must inform steroid decisions. Incorporating biomarkers like IL-6 levels or T-cell exhaustion markers may help identify patients in whom steroids would blunt efficacy versus those where risk is minimal. Multidisciplinary input, especially from immunologists and oncologists, ensures tailored care.
4. Steroid-Sparing Strategies: Where appropriate, consider alternative immunomodulators (e.g., infliximab, vedolizumab, mycophenolate) in patients with steroid-refractory or recurrent irAEs to minimize prolonged steroid exposure without compromising immunotherapy benefits.

In essence, steroids must be wielded like a scalpel, not a sledgehammer—precise, purposeful, and patient-specific—to safeguard both quality of life and the promise of cure.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Improved efficacy of cancer immunotherapy while minimizing the immunosuppressive effects of corticosteroids through personalized steroid administration.

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. The Steroid-Immunotherapy Paradox

Timing Matters:

Pre-IO Steroids (e.g., for brain edema): Reduce T-cell activation avoid unless life-threatening.

Concurrent Steroids (10mg prednisone/day): Linked to poorer PFS in NSCLC (KEYNOTE-042).

Post-IO irAE Management: Necessary for grade 2 toxicities (e.g., colitis) but taper rapidly.

2.Balancing Act: Maximizing Safety & Efficacy

A. "Steroid-Sparing" Protocols

Prophylactic Tocilizumab: For high-risk patients (pre-existing autoimmunity) to prevent irAEs, avoiding steroids.

Fecal Microbiota Transplant (FMT): For steroid-refractory colitis restores gut microbiome, reduces steroid dependence.

B. "Time-Locked" Steroid Dosing

Circadian AI Dosing: Administer steroids at 4 AM (peak endogenous cortisol) to minimize immune disruption.

Pulsed High-Dose for irAEs: 48-hour methylprednisolone bursts (1g/day) rapid taper to <5mg/day within 7 days.

3. Personalized Steroid Strategies: "Immuno-Atlas" Biomarker Profiling

Baseline Lymphocyte Mapping: Patients with high CD8+/Treg ratios can tolerate steroids better (retain anti-tumor response).

Liquid Biopsy Guidance: Rising ctDNA during steroid taper? Hold steroids, escalate IO

4.Implementation: The "Steroid Score" Clinic

Pre-IO Risk Stratification:

Low Risk (Steroid Score A): Avoid prophylactic steroids.

High Risk (Steroid Score C): Non-steroid alternatives (e.g., IVIG for fatigue).

Real-Time Monitoring: CORT-Test Strips: Salivary cortisol levels to guide taper speed.

Patient Empowerment: "Steroid Diary" App: Tracks mood/energy/symptoms, flags over/under-use

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
The primary outcome of the above solutions is to preserve the efficacy of immune checkpoint inhibitors (ICIs) by minimizing unnecessary steroid exposure—especially during the early phase of treatment—and promoting steroid-sparing strategies (e.g., for antiemetic prophylaxis during chemoimmunotherapy). This approach aims to balance optimal cancer control with effective toxicity management, thereby improving overall patient outcomes in immunotherapy 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.):

Steroids can impair the efficacy of cancer immunotherapy by suppressing immune activation and T-cell function—key mechanisms through which immune checkpoint inhibitors (ICIs) work. Their use,

especially early or at baseline, has been associated with reduced response rates and inferior survival in multiple cancers.
1. Optimal Timing of Steroid Administration: Avoid steroid use at the start of immunotherapy unless absolutely necessary (e.g., for symptomatic brain metastases). Late-onset steroid use for immune-related adverse events (irAEs), when ICIs have already primed the immune system, has a lesser negative impact. Short duration and rapid tapering are crucial to minimize immunosuppression.
2. Balancing Toxicity Management and Efficacy: Use the lowest effective dose for the shortest duration when managing irAEs. In steroid-refractory cases, consider early introduction of steroid-sparing immunosuppressants like infliximab or mycophenolate to preserve ICI efficacy. Monitor for early irAE symptoms to intervene promptly with minimal immunosuppression.
3. Considerations in Chemoimmunotherapy: Routine antiemetic regimens using dexamethasone in chemoimmunotherapy may blunt immune responses. Employ steroid-sparing antiemetic protocols, such as olanzapine-containing regimens, to reduce unnecessary corticosteroid exposure while maintaining symptom control.
4. Individualized Steroid Use: Personalize decisions based on tumor type, disease burden, irAE risk, and patient comorbidities. Incorporate multidisciplinary input and emerging biomarkers to guide safer steroid strategies.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Optimization of Steroid usage with immunotherapy in cancer 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.):
Steroids like prednisone suppress the immune system, potentially weakening immunotherapy's effectiveness, which relies on T-cell activation. Drugs like pembrolizumab boost immunity against cancers (e.g., NSCLC), but steroids reduce T-cell activity and cytokine release, lowering response rates. Studies show high-dose steroids (>10 mg prednisone daily) at baseline cut progression-free survival in anti-PD-1 therapy. They alter the tumor microenvironment, limiting immune infiltration. However, short-term, low-dose steroids for managing immune-related adverse events (irAEs) like pneumonitis often have negligible impact, balancing efficacy and safety in resource-constrained settings like India. When to Administer Steroids and Risk-Benefit Steroids are used to treat severe irAEs (e.g., grade 3-4 colitis, hepatitis), affecting 10-20% of immunotherapy patients, with ESMO recommending 1-2 mg/kg prednisone, tapered over 4-6 weeks. They also manage symptoms like brain edema or premedicate in chemo-immunotherapy combos. Benefits include rapid irAE control, preventing organ damage, and sustaining therapy. Risks involve reduced immunotherapy response, infections (20% higher risk), and side effects like diabetes, especially in India with high TB prevalence. Steroids are justified for severe irAEs but avoided for mild cases, using alternatives like antihistamines. Patient factors, like comorbidities, guide decisions. Optimizing Steroid Use To optimize steroids, use low doses (0.5-1 mg/kg) for moderate irAEs, tapering quickly (4-8 weeks) to preserve immunotherapy benefits. Monitor biomarkers (e.g., IL-6) to tailor doses, affordable at ₹5,000-₹10,000 in India. Use steroid-sparing drugs like infliximab for refractory cases. Tumor boards ensure precise steroid use, while patient education

aids early irAE detection. Prophylaxis against infections and India-specific guidelines addressing TB risks enhance safety, ensuring effective immunotherapy for 1.5 lakh cancer patients annually.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Many non-small cell lung cancer (NSCLC) patients encounter clinical situations that necessitate the simultaneous use of both immunotherapy and corticosteroids. Common scenarios include malignant spinal cord compression and brain metastases. Although the mechanisms of action of immunotherapy and steroids are generally considered antagonistic, their concurrent use is sometimes unavoidable. Even, patients undergoing CAR T-cell therapy often receive steroids to manage cytokine release syndrome yet still retain an adequate number of functional CAR T-cells following steroid administration. However, in NSCLC, there is currently insufficient data to determine the impact of corticosteroid use on the efficacy of immunotherapy. Our study aims to evaluate the effects of steroids on immunotherapy outcomes and to identify the optimal timing for steroid administration in patients receiving immunotherapy.

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.):
Patients with metastatic non-small cell lung cancer (NSCLC) undergoing treatment with immunotherapy and presenting with clinical indications for corticosteroid use will be randomized into three study arms:
Arm A: Steroids administered 6 hours prior to immunotherapy.
Arm B: Steroids administered concurrently with immunotherapy.
Arm C: Steroids administered 6 hours after immunotherapy (hypothesized to “prime” the immune system, potentially sustaining immune activity despite steroid exposure).
Most seroids have their peak action after 1-2 hours of administration. Patients in each arm will be monitored using the following immune-related biomarkers:

- T-cell receptor (TCR) sequencing via next-generation sequencing (NGS) of peripheral blood, to assess clonal T-cell expansion indicative of an active immune response.
- Inflammatory cytokine profiling through ELISA, to reflect systemic immune activation.
- Neutrophil-to-lymphocyte ratio (NLR), with higher values suggestive of an immunosuppressive milieu.

These parameters will be assessed before each treatment cycle to evaluate dynamic immune responses and guide interpretation of immunotherapy efficacy in the context of steroid timing.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To optimize the use of steroids in cancer immunotherapy by minimizing their impact on treatment efficacy while effectively managing immune-related adverse events, through strategic timing, dosage control, and the integration of alternative immunosuppressive therapies and biomarkers.

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.):
Steroids play a dual role in cancer immunotherapy, offering symptom control while potentially impairing treatment efficacy. The timing of steroid administration is critical in determining their effect on immune response. Timing of Steroid Use:
Early administration (within the first 4–6 weeks of starting immunotherapy) is linked to reduced treatment efficacy. This is because early use can inhibit T-cell priming and infiltration—key mechanisms for an effective immune response.
Late administration, typically in response to immune-related adverse events (irAEs), tends to have less negative impact on immunotherapy efficacy. Prophylactic use of steroids should be avoided unless clearly indicated, such as for brain metastases or cerebral edema. Delaying steroid use allows the immune system time to activate and respond to the tumor.
Balancing Efficacy with Side Effect Management:

- Use the lowest effective dose and taper steroids as tolerated.
- For mild to moderate irAEs, consider non-steroidal immunosuppressants (e.g., mycophenolate mofetil, infliximab) as alternatives.
- Employ biomarkers (lymphocyte counts, cytokine levels, T-cell activation markers) to tailor the intensity of immunosuppression and optimize therapeutic outcomes.

This balanced approach helps preserve the benefits of immunotherapy while effectively managing its side effects.

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Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Title: Evaluating the Impact of Corticosteroids on Immunotherapy Efficacy in Non-Small Cell Lung Cancer (NSCLC)
Background: In the management of non-small cell lung cancer (NSCLC), patients frequently face clinical conditions that necessitate the concurrent use of immunotherapy and corticosteroids. Common indications include malignant spinal cord compression, brain metastases, and other emergent complications. While the immunosuppressive nature of corticosteroids is theoretically antagonistic to the immune-stimulating effects of immunotherapy, their simultaneous use is often clinically unavoidable. Interestingly, in the context of CAR T-cell therapy, corticosteroids are administered to manage cytokine release syndrome, with many patients retaining functional CAR T-cell activity. However, in NSCLC, the impact of corticosteroids on the efficacy of immune checkpoint inhibitors (ICIs) remains poorly defined.

Rationale: This study aims to explore whether the timing of corticosteroid administration influences the immune response and clinical outcomes in patients with NSCLC undergoing immunotherapy. We hypothesize that strategic timing of steroid use may minimize immunosuppression or even prime the immune system, preserving the therapeutic potential of immunotherapy.

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 Patients with metastatic NSCLC receiving immune checkpoint inhibitors and requiring corticosteroids for clinical indications will be randomized into three arms:

- Arm A: Steroids administered 6 hours prior to immunotherapy
- Arm B: Steroids administered concurrently with immunotherapy
- Arm C: Steroids administered 6 hours after immunotherapy (Hypothesized to promote immune priming and sustain immune activation despite steroid exposure)

Biomarker Assessments Immune response will be monitored using a panel of biomarkers at baseline and before each treatment cycle: T-cell Receptor (TCR) Sequencing (via Next-Generation Sequencing of peripheral blood): To assess clonal T-cell expansion as a surrogate for immune activation. Cytokine Profiling (via ELISA): To quantify pro- and anti-inflammatory cytokines, reflecting systemic immune dynamics. Neutrophil-to-Lymphocyte Ratio (NLR): An elevated NLR is associated with an immunosuppressive tumor microenvironment and worse outcomes.
Endpoints:

- Primary Endpoint: Impact of steroid timing on objective response rate (ORR) to immunotherapy
- Secondary Endpoints: Progression-free survival (PFS), Overall survival (OS), Dynamic changes in immune biomarkers

Conclusion This study seeks to clarify the immunological and clinical implications of corticosteroid use in the setting of immunotherapy for NSCLC. By investigating timing-dependent effects, we aim to inform best practices for managing steroid-requiring complications without compromising the efficacy of immune checkpoint inhibition.

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Tamil Nadu

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
To develop approaches that can help balance potential benefits of managing side effects with the potential reduction in immunotherapy efficacy. To develop solutions on individualizing steroid administration in cancer care.

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.):
Optimal timing of steroid administration: As late as possible from ICI administration to avoid reduced ICI efficacy Avoid steroid as premedication, if given for autoimmune conditions, use dose as low as possible (less than 10mg) or utilise steroid sparing medications.
Steroid and ICI: Steroids are anti-inflammatory drugs which have immunosuppressive effects through reduced IL2 mediated T cell activation and upregulating the activity of Treg cells. ICIs work by

activating the immune system by inhibiting immune checkpoints(PD1/CTLA4/LAG). So steroids are antagonistic to ICI , but steroids are a part and parcel of oncology used in managing various situations, heres an approach to minimise their interactions
1.CINV - Use steroid sparing regimens like (NK1A + 5HT blockers + olanzapine) while using chemo immunotherapy.We have evidence for its efficacy also in highly emetogenic chemotherapy (Radhakrishnan et al - study by cancer institute chennai)
2.Brain mets - Use RT for symptomatic brain mets, use bevacizumab for brain edema, use steroid only if it is refractory to both
3.Cancer cachexia and fatigue - avoid steroids as much as possible. Use other drugs like olanzapine and megestrol acetate for cachexia and CBT, non-pharmacologic management for fatigue
4. Autoimmune conditions and hypersensitivity reactions - steroids can be used wisely at low doses 10mg/day, studies have shown that in such cases steroids have no negative effects on ICI efficacy.

Steroid sparing drugs for IRAEs: Steroids can also used for management of IRaes which are more than grade 2 toxicity. Data shows that steroids use in IRaes does not blunt ICI efficacy, but dose and duration should be as low as possible. Studies are ongoing to use targeted therapy like INF alpha antagonists, IL6 inhibitors and immunomodulators in first line management of IRAes which can further help reduce interaction of ICI and steroids.

Full Name:
Amol Sitaram Rathod

Name of the Institution:
PD Hinduja National Hospital and Medical Research Centre

State:
Maharashtra

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Delay steroids as much as possible

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)

A- Steroids Decreases efficacy, overall response rate, decreases PFS, OS with IO in NSCLC

- Increased time to steroids increases PFS, OS.
- Metastatic setting has no effect, while in adjuvant setting has less efficacy
- Overall Shorter time to steroid, higher dose and additional Immunosuppression predicts drop in efficacy of IO. But on other hand, no irAE has ORR <20%, therefore irAE predicts higher response of IO. Should balance off the effect of steroid on IO.

B- For Anti CTLA-4 IO, after 2 months
C- For anti PD-L1 IO, after 1 month

2)

A- Individualized steroid use
B- Regular investigation (6 weekly) TSH, 8AM cortisol, ACTH, LFT, inflammatory markers
C- Increase spacing between doses. Dropping 1-2 doses, specifically in metastatic setting.
D- Desensitizing protocol for IO in patient having high tendency for irAE.

3)

A- Dexamethasone free anti-emetic regimen if combined with highly emetogenic chemotherapy regimen
B- Low dose steroids with rapid tapper for lower grade irAE
C- Delaying higher dose of steroids as much as possible.
D- Higher doses of IO

Full Name:
Pearl

Name of the Institution:
KMC Medical College

State:
Uttar Pradesh

Objective of your solution: (Briefly define the primary outcome of your solution to this challenge):
Steroids and Immunotherapy in Cancer: Finding the Right Balance
1. Imp to manage symptoms or treatment-related side effects
2. When to start and when to stop is also acting like targeted therapy or I should say
3. Cumulative approach for our immunotherapy to act in our bodies
4. Taper quickly, when possible, tailor the treatment
5. Prophylactic steroid use should be avoided unless clearly indicated.
6. Brain metastases, steroids are often unavoidable here, delaying immunotherapy by a few days may help mitigate risk

Conclusion
Steroids aren't the enemy they are an essential tool in oncology.
But like any tool, they must be used with care.
The goal isn't to eliminate steroids from immunotherapy, it's to use them wisely, time them right, and tailor them to the patient's story. its balance with treatment plays a critical role

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:
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 effects of steroids on the efficacy of immunotherapy.

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.):
Concurrent use of steroids and immunotherapy undermine the efficacy of immunotherapy by impairing IL2 mediated effector T cell activation and increasing regulatory T cells.
Factors determining the impact of steroids on immunotherapy
1.Baseline steroid dose - > 10 mg within 24 hours of initiation of immunotherapy - worse outcomes
2. Prolonged steroid dose
3. Early steroid use l- worse outcomes

Solutions
1. Steroid sparing approaches
2. Delaying steroid exposure
3. Short delays of ICI induction to facilitate steroid taper

Steroid sparing approaches
1. Radiation therapy in symptomatic brain metastases avoiding steroids
2. Corticorelin acetate and Bevacizumab - alternative to steroids in cerebral edema and melanoma brain metastases respectively
3.Steroid alternatives for IRAE - monoclonal antibodies targeting IL6, TNFalpha, JAK, BTK
4, Hydroxychloroquine in ICI induced inflammatory arthritis
5. Abatacept, a CTLA4 fusion protein in ICI associated myocarditis.

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):
Use of steroids with immunotherapy will be used more judiciously.

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.):
Steroids reduce efficacy of immunotherapy. To avoid steroids prior or later to immunotherapy unless being used to side effects due to immunotherapy. Give a list of indications for steroids use with immunotherapy.

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): Steroids are a necessary but potentially risky tool in the immunotherapy arsenal. Their use should be nuanced, with attention to timing, dose, and patient context. When managed wisely, steroids can safely support immunotherapy without significantly undermining its benefits.

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.):

Impact of Steroids on Cancer Immunotherapy Introduction Steroids can have a significant impact on cancer immunotherapy, as they modulate the immune response and potentially affect the effectiveness of immunotherapeutic treatments. The use of steroids is often necessary to manage immune-related adverse events (irAEs), but inappropriate use can diminish therapeutic benefits. This document outlines the optimal timing of steroid administration, strategies to balance their benefits and risks, and approaches for individualizing steroid use in cancer care.

1. Optimal Timing of Steroid Administration Timing plays a pivotal role in determining whether steroids will significantly impact the efficacy of immunotherapy.

- Before Initiation of Immunotherapy: High-dose baseline steroids (>10 mg prednisone equivalent/day) used prior to immunotherapy initiation are associated with poorer outcomes.
- Early During Immunotherapy (within first 30 days): - Steroid use early during treatment may impair T-cell activation and reduce immunotherapy efficacy.
- Later During Therapy: - Steroid use for irAEs after the initial priming phase is less likely to compromise immunotherapy outcomes.

2. Balancing Symptom Management with Preserving Efficacy Strategies include:

- Use steroid-sparing agents where possible (e.g., infliximab, tocilizumab).
- Use the lowest effective dose and taper as soon as feasible.
- Employ multidisciplinary teams for toxicity management.
- Monitor biomarkers to guide steroid use and prevent overt immunosuppression.

3. Individualizing Steroid Use in Cancer Immunotherapy Considerations include:

- Patient-specific factors (e.g., comorbidities, age, performance status).
- Tumor-specific factors (e.g., tumor type, mutational burden).
- Treatment-specific considerations (e.g., CAR-T cell therapy side effects).