Malignancy in Patients with Psoriasis: Understanding the Risk and Appropriate Management Strategies

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The attributable risk specific to psoriasis is difficult to isolate.

- A 16% increased risk of malignancy in psoriasis patients compared to the general population.¹
  - Variable adjustment for malignancy risk factors

Population-based studies form the UK, Taiwan & Korea confirm an increased risk of malignancy.¹-³
- Risk persists after adjustment for malignancy risk factors
- Driven by lymphoproliferative malignancies and keratinocyte carcinomas
- No increased risk seen in the pediatric population⁴

Risk of Lymphoproliferative Malignancies

- An elevated risk of lymphoproliferative malignancies was reported in several studies.¹-⁴
  - Persists after adjustment for age, sex, treatment and excluding people who develop CTCL
  - Risk is strongest between severe psoriasis & Hodgkin’s lymphoma²-³
  - No increased risk of leukemia seen²-⁵

Risk of Skin Cancer

- Baseline risk difficult to assess due to confounding from skin type and treatments
- An increase risk of keratinocyte carcinoma has been seen in meta-analyses and population-based longitudinal cohorts.³-⁵
  - HR: 1.12 (1.07 – 1.16)
  - The risk of melanoma is conflicting.

Baseline Risk of Malignancy

- Patients with psoriasis appear to have a small, but significantly elevated risk of malignancy.
  - Driven by increased rates of lymphoma and skin cancer
  - Likely due in some part to other risk factors for malignancy (smoking, alcohol use, obesity)
  - Encourage patients to complete age appropriate cancer screening.
  - A full skin exam should be incorporated into psoriasis visits.

Summary

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**Risk of Malignancy Associated with Phototherapy**

- **Oral Psoralen + UVA (PUVA)**
  - The PUVA Follow-Up Study
    - >350 PUVA treatments increased the risk of SCC but NOT BCC
    - An increased risk of melanoma was delayed (>15 yrs after initiation of treatment) and increased over time.

- **Oral PUVA & SCC**
  - Risk of SCC persists for up to 15 years
  - Dose-dependent increased risk on non-exposed skin
  - 30% reduction in SCC from oral retinoid treatment
  - Actinic & pigmentedary changes of exposed AND non-exposed skin

- **nbUVB in the PUVA Cohort**
  - Sub-analysis of treatment with < 100 PUVA txs + UVB
  - High dose UVB (> 300 tx) increases the risk of BCC and SCC
    - >25 years of prospective follow-up
    - Most apparent on non-head/neck sites
    - 1 PUVA treatment has 7X> carcinogenic risk compared to 1 nbUVB tx.

- **UVB monotherapy**
  - No increased risk of skin cancer overall in patients receiving <100 treatments
  - Long latency time for the development of KC may limit detection in the current studies.

- **Summary**
  - Patient treated with high dose PUVA (>350 txs) have an increased risk of SCC and melanoma.
  - nbUVB alone (< 100 tx) is not associated with an increased risk of skin cancer.
  - Patients with a history of long term phototherapy should receive regular FBSE.

**Risk of Malignancy Associated with Systemic Therapies**

- Methotrexate (≤30 mg/week) monotherapy is not associated with an increased risk of malignancy. 1-3
- Cyclosporine increases the risk of skin cancer in patients who received PUVA, concurrent MTX or in pts on tx > 2 yrs. 4
- Acitretin is used for KC prevention in high risk populations. 5

**Traditional Systemic Therapies**

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**TNF Inhibitors & Systemic Malignancy**

- In 2006, a meta-analysis of RCTs for RA suggested an increased risk of malignancy associated with infliximab and adalimumab (OR 3.7, 95% CI 1.0–13.2). 1
- 3 subsequent meta-analyses did NOT confirm this risk. 2-4
- Using population-based data from Kaiser Permanente Northern California (KPNC), there was no increased risk of malignancy in psoriasis patients treated with TNF inhibitors compared to those never exposed. 5
- An analysis of older adults (>65 yrs) did not find an increase in cancer in TNF users compared to non-users. 5

**TNF Inhibitors & Melanoma**

- In increased risk of melanoma was seen in adalimumab-treated psoriasis patients compared to the general population. 2
- There was no risk in the real-world data from KPNC. 2

**TNF Inhibitors & Keratinocyte Carcinoma**

- A meta-analysis of RCT data did not find an increased risk of KC in patients treated with TNF inhibitors compared to placebo. 6
  - The short follow-up time (< 20 wks) in this study may not have allowed for adequate detection
- In the KPNC cohort, KC rates were 42% higher among individuals ever exposed to a biologic. 6
  - Average Follow-Up: 5.9 years
  - The risk was largely driven by increased risk of SCC
  - The analysis was adjusted for a prior history of phototherapy 6

**Other Biologic Agents**

- **Ustekinumab:**
  - Data: prospective registries
  - Malignancy rate comparable to general population. 7,8
- **IL-17 Inhibitors:**
  - Data: pooled phase III
  - Malignancy rate < or = the psoriasis population. 9,10
- **Guselkumab:**
  - Data: phase II and phase II
  - No increased incidence vs placebo arms 9
- **Apremilast:**
  - Data: Phase III clinical trial
  - Rate of malignancy comparable to the general population 7,10

**References:**

No increased risk of systemic malignancy or melanoma in psoriasis patients exposed to TNFi.

There may be an increased risk of SCC in psoriasis patients exposed to TNFi.

No safety signals in new agents; but, larger and longer-term studies are needed.

No increased risk of recurrent malignancy in patients receiving TNF inhibitors compared to other immunosuppressive therapy and no immunosuppression. A slightly higher recurrence rate was seen in combination immunosuppression. There may be cancer-specific associations not identified in this analysis.

RA patients with a history of breast cancer, treated with TNF inhibitors did not have an increased recurrence rate compared to those not exposed to TNF inhibitors.

Median Time to TNF inhibitor treatment: 9.4 years
Average Follow up: 5 years
Generalizability to women with a very recent or a poor prognosis of breast cancer is unknown

No association between the use of TNF inhibitors following surgery and the risk of breast cancer recurrence in RA/IBD patients.

An increased recurrence rate has not been seen in patients with a history of malignancy, treated with TNF inhibitors.

Available data is limited.

Generalizability to all cancer types, aggressive subtypes and recent malignancies is unknown.

Each patient should be considered on an individual basis in conjunction with an oncologist.

Patients with a history of malignancy should be co-managed with other specialists to understand their personalized risk/benefit ratio for psoriasis treatments.