The Risk Of KC In Psoriasis Patients Receiving Biologics Compared To Conventional Systemic Therapies

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The risk of keratinocyte carcinoma (KC) in psoriasis patients receiving biologic therapy compared to conventional systemic therapy: results from the British Association of Dermatologists Biologic Interventions Register (BADBIR)

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Background

- Biologic therapies for treatment of moderate-to-severe psoriasis
  - Targeted suppression of key immune-modulators in disease pathogenesis
  - Cost-effective
- Questions remain regarding long-term safety of biologic therapies
  - Cancers are rare and typically have a long latency to development
  - KC, comprising basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC), have shorter latency
  - Most common cancers with incidence of KC increasing in general population
- Systematic review: risk of KC following exposure to biologic therapies in psoriasis patients poorly understood
- Incidence of KC identified using the Medical Dictionary for Regulatory Activities preferred terms of cancers
- Linkage to national registers for cancer, death and hospital episodes
- Biologic mechanisms (Stelara vs TNFi)

Aims

To determine whether the rate of KC, specifically BCC and cSCC, is increased in patients with psoriasis exposed to biologic therapy compared with those only exposed to conventional therapies

Methods

BADBIR Study Design

- Prospective pharmacovigilance register of patients with moderate-to-severe psoriasis
- Recruited from 157 dermatology centres in the UK and Republic of Ireland
- Patients must be starting or switching to one of the conventional or biologic therapies in Figure 1
- Clinical follow-up (therapy changes; disease severity; adverse events) recorded every 6 months for the first three years, and annually thereafter
- Linkage to national registers for cancer, death and hospital episodes

Statistical Methods

- Baseline characteristics by cohort (Chi

2
-test; * two-sample T-test)
- Crude and adjusted incidence rates (IRs) per 1000 person-years calculated for KC, BCC, and cSCC in biologic and conventional cohorts
- Propensity score weighted Cox-proportional hazard models estimated the hazard ratio (HR) for developing a first KC, BCC, and cSCC
- Confounding factors: age, sex, previous PUVA and ciclosporin

Analysis Plan

Figure 1: BADBIR Cohorts

Results

- A total of 14,665 patients were registered to BADBIR as of 01/09/2017
  - Of those, 6,000 (41%) completed at least one follow-up, were biologic-naïve at registration, had chronic plaque psoriasis, were of white ethnicity with a Fitzpatrick skin type 1-4, and had no personal history of cancer
  - Registrations to the biologic cohort totaled 5289 (30%) with 3062 (35%) patients registering to the conventional cohort

Table 1: Baseline characteristics of the biologic and conventional cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Biologic Cohort</th>
<th>Conventional Cohort</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total registrations</td>
<td>5289 (100%)</td>
<td>3062 (100%)</td>
<td>---</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45 (35, 53)</td>
<td>44 (33, 54)</td>
<td>0.173†</td>
</tr>
<tr>
<td>Females</td>
<td>2000 (38%)</td>
<td>1261 (41%)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Baseline PASI</td>
<td>14.0 (10.8, 19.2)</td>
<td>14.0 (11.1, 18.9)</td>
<td>0.244*</td>
</tr>
<tr>
<td>Achieving</td>
<td>1976 (37%)</td>
<td>1946 (64%)</td>
<td>—</td>
</tr>
<tr>
<td>Baseline BDI</td>
<td>18.2 (12.2)</td>
<td>18.2 (12.2)</td>
<td>0.513</td>
</tr>
<tr>
<td>Achieving</td>
<td>2095 (40%)</td>
<td>2095 (40%)</td>
<td>—</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>20 (12, 30)</td>
<td>20 (12, 30)</td>
<td>0.000†</td>
</tr>
<tr>
<td>Achieving</td>
<td>44 (34, 54)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Follow-up time (months)</td>
<td>2.6 (1.3, 4.1)</td>
<td>0.8 (0.3, 1.6)</td>
<td>0.002†</td>
</tr>
<tr>
<td>Previous systemic therapies; median (IQR)</td>
<td>7 (5, 12)</td>
<td>11 (5, 12)</td>
<td>0.002†</td>
</tr>
<tr>
<td>Pui at baseline</td>
<td>1132 (22%)</td>
<td>298 (10%)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Registration</td>
<td>England</td>
<td>4183 (94%)</td>
<td>2543 (89%)</td>
</tr>
<tr>
<td>Country</td>
<td>Northern Ireland</td>
<td>309 (6%)</td>
<td>125 (4%)</td>
</tr>
<tr>
<td>Scotland</td>
<td>322 (6%)</td>
<td>118 (4%)</td>
<td>—</td>
</tr>
<tr>
<td>Wales</td>
<td>333 (6%)</td>
<td>109 (4%)</td>
<td>—</td>
</tr>
<tr>
<td>Previous</td>
<td>PUVA</td>
<td>1628 (30%)</td>
<td>751 (24%)</td>
</tr>
<tr>
<td>Therapies</td>
<td>PUVA and ciclosporin</td>
<td>600 (11%)</td>
<td>146 (5%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>Never Smoked</td>
<td>2053 (42%)</td>
<td>1334 (44%)</td>
</tr>
<tr>
<td>Status</td>
<td>Ever Smoker</td>
<td>3327 (65%)</td>
<td>1048 (35%)</td>
</tr>
</tbody>
</table>

Incidence Rates

- A total of 74 patients registering to the biologic cohort reported a first KC (40 BCC only; 30 cSCC only) with 21 patients diagnosed with a first KC (11 BCC only; 7 cSCC only) in the conventional cohort (Figure 2)
  - Seven patients (4 biologic cohort; 3 conventional cohort) diagnosed with first BCC and cSCC on same date
  - BCC were more commonly reported than cSCC in both cohorts; however, the incidence of BCC for patients receiving biologic therapies was lowered after adjusting for confounding factors (Figure 2)

Figure 2: Incidence rates per 1000 person-years and Cox-proportional hazard ratios for the risk of KC

Cox-Proportional Hazard Ratios

- An adjusted HR of 1.10 (95% CI 0.66, 1.82) was calculated for the development of a first KC in the biologic cohort (Figure 1)
  - Adjusted HRs of 0.91 (95% CI 0.49, 1.70) and 1.16 (95% CI 0.56, 2.43) were calculated for the first BCC and cSCC, respectively
  - Patients were not at significantly higher risk of developing a KC in the biologic cohort, after adjusting for confounding factors

Discussion

- In BADBIR there was no significantly increased risk of developing a KC, BCC, or cSCC following exposure to biologic therapies after adjusting for confounding factors

Strengths

- Incident user design (biologic cohort); representative of clinical practice in the UK and Republic of Ireland

Limitations

- Not possible to explore the risk of cumulative exposure to ultraviolet therapies

Future Work – Sensitivity Analyses

- Baseline characteristics of cohort
- Age categories (<40 years; 40-59 years; >60 years)
- Latency periods (excluded KC diagnosed within 6, 9 & 12 months of initiating therapy)
- Smoking status (ever/never)
- PUVA and ciclosporin

References

2. Iskandar et al. BJD 2017;177(5):1410-1421

Conflicts Of Interest

Authors KL, HA, AAS, RP, MMS and ACG declare no conflicts of interest.

Financial Disclosures:

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