

# Melanocytic Lesions in Children and Adolescents

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# Melanocytic Nevus in Children

- Congenital melanocytic nevus (CMN) present at birth in 1-2% of children
  - Increased risk of melanoma in large CMN
- Acquired nevi develop in childhood
  - Number of nevi increase until age ~40
  - Genetics and sun exposure
  - Nevi undergo growth/maturation
- Melanoma most frequently arises *de novo*
  - Can arise *within* acquired/congenital nevus
  - No clear evidence that nevi “transform into” melanoma

# Melanoma in Children/Adolescents: Risk Factors

- Melanoma in preadolescent children rare, not associated with typical adult risk factors
  - May be non-white, arise in sun protected areas, no family history, not associated with dysplastic nevi
- Melanoma in teenagers increasing in incidence, more like adult melanoma
  - More likely fair, family history, atypical nevi

# Melanoma in Children/Adolescents: Presentation

- Clinical presentation in preadolescent children differs from adults
  - More frequent nodular histology, head, face, neck primaries, metastatic
- Sentinel lymph node biopsy (SLNB) performed to assess prognosis/staging
- When matched for depth and stage, prognosis and mortality similar to adults

# Spitz Nevus

- Benign melanocytic nevus with characteristic histology, previously known as “benign juvenile melanoma”
- Typically, pink-red papule, < 1 cm in diameter
- Usually on face, limbs (may be pigmented)
- May appear suddenly, grow rapidly
- Microscopic foci reported in draining lymph node (also seen with blue nevi)
- May be difficult to distinguish from melanomas with “spitzoid” histologic appearance

# Atypical Spitzoid Melanocytic Tumor (ASMT)

- Subset of Spitz-like growths with certain features associated with melanoma (eg mitoses)
- Interobserver agreement regarding diagnosis is poor, even among experts
- 28-50% of patients with ASMT who undergo SLNB have positive LN
  - Positive LN not diagnostic of melanoma
- Prognosis in ASMT, including those that are thick and/or with positive SLNB, is favorable unlike melanoma (*Busam, 2009; Ludgate, 2009*)

# Case #5636222

- 13 yr old female with 7.5 x 2 cm congenital melanocytic nevus (CMN) on buttock
- Applied tacrolimus ointment to popliteal fossae, elbow folds and lateral neck for atopic dermatitis
- Diagnosed with melanoma within CMN on buttock, +SLNB

# Case #5636222

- *Tacrolimus not applied near CMN*
- *Large CMN is known risk factor for melanoma*



# Case #5049703/5965099

- 12 yr old female, history of vitiligo
- Applied tacrolimus ointment for ~3-4 wks to 4-5 mm papule on forearm thought to be molluscum
- Lesion grew, surface eroded and was biopsied
- Diagnosed as atypical spitzoid melanocytic neoplasm vs. melanoma
- Treated as melanoma with local excision, enrolled in vaccine trial
- Alive with NED as of March, 2010
- *Initially considered as two cases; recently confirmed to be same case*

# Case #5049703/5965099

- *Tacrolimus applied for short period of time*
- *Appearance as molluscum/pyogenic granuloma, spitzoid pathology*
- *Lack of recurrence after 5 years*
  - *Is this an atypical spitzoid melanocytic tumor?*

# Case #5850928

- 4 yr old male with eczema treated with tacrolimus ointment and pimecrolimus cream beginning at age 4 months
- “Reddish pigmented lesion” on leg diagnosed as severely atypical spitzoid neoplasm, borderline
  - +SLNB, single microscopic focus
  - All other nodes negative on dissection
- Treated with excision and interferon

# Case #5850928

- *Clinical appearance, pathology and single +LN all consistent with atypical spitzoid melanocytic tumor*

# Pediatric Safety Analysis

## Pediatric Post-Marketing Exposure

- Estimated US exposure: 927,000 patients through 2009

Source: SDI's Total Patient Tracker (TPT)

- Reported malignancies through Jan, 2010:
  - 31 (Global)
  - 18 (US)

# Global Long-term Safety Studies

- Four ongoing studies: 3 in Japan, 1 in US/EU/Canada
- Total planned enrollment
  - 2400 patients in Japan
  - 8000 patients in the US/EU/Canada
- Current enrollment (March 2010)
  - Over 2500 patients in Japan
  - Approximately 5300 patients in the US/EU/Canada
- Duration of follow-up: 10 years for all studies
- Reports of Malignancy
  - 3 US/EU/Canada study
  - 0 Japanese studies

# Protopic: Current US PI Overview

- Malignancy labeled:
  - Rare cases of malignancy (eg skin and lymphoma) have been reported
  - Causal relationship has not been established
  - Protopic use should be avoided in pre-malignant and malignant skin conditions
  - Neoplasms are identified and include “malignant melanoma”
  - Do not use in children under 2
- Included in:
  - Boxed Warning
  - Warnings
  - Precautions: General
  - Adverse Reactions and Post-Marketing Events/Neoplasms

# Protopic: Current US PI Overview

## Infections labeled:

- Precautions: bacterial and viral skin infections
  - Eczema herpeticum (Kaposi's varicelliform eruption), herpes infections
- Adverse Reactions and Post-Marketing Events
  - Fungal dermatitis, cellulitis, impetigo, abscess, warts, osteomyelitis, septicemia



# Conclusions

- Risk/benefit profile remains unchanged for use of Protopic in moderate to severe AD
- Boxed Warning and Warnings contains appropriate risk information related to malignancies (eg skin and lymphoma) and infections
- Post-marketing surveillance has identified reports of new neoplasms