Adenovirus mediated IFN-\(\gamma\) expression in cutaneous lymphomas: monitoring of local and systemic events

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Skin cancer unit
German Cancer Research Center
Heidelberg, Germany
Immune intervention in MF using a third generation adenoviral vector system

Epidermis derived viability factors

Epidermis

Macrophage

TH 1

TH 2

PBMC

NK

CD8

T-LY

IL-5

IL-10

IFN-γ

Adeno

Immunosuppression

eosinophilia

IgE IgA

IgG

IK
The vector: Adeno-IFN-γ
tg1042 (Transgene)

Local IFN-γ production

The recipients:
H-CAR expression in CTCL
Phase I:
TNM stage Ib or higher
Failure of local tumor control by at least 2 first line treatments
Dose-Escalating
  3 Dose levels: 3X10E9, 3X10E10, 3X10E11 tp
  3 Patients / dose level

TG1042.01 : Cutaneous Lymphomas

Adenovirus-mediated intralesional interferon-γ gene transfer induces tumor regressions in cutaneous lymphomas
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3X10E11 tp  12 additional patients March 2002- Sept. 2004
Inclusion criteria:
Histologic proof of CTCL or CBCL
Performance status 0,1 or 2 on the ECOG scale
TNM stage Ib or higher
at least 2 first-line treatments
No systemic chemo- or immunotherapy within preceding 3 weeks
Minimum life expectancy > 3 months
Adequate hematologic, hepatic and renal function

Exclusion criteria:
• HIV+ or other active systemic infections
• Serious concomitant systemic medical disorders
• Concomitant corticosteroid therapy
• Major surgery in previous 3 weeks
• Pregnancy
• Other therapies for lymphoma
Treatment plan

1. treatment cycle
2. treatment cycle, etc.

Baseline

Tumor assessment

d1

d8

d15

d29 (d1)
d8

d15

d29

Tumor assessment
Side effects

Mainly locally: erythema, oedema, pain
Flu-like symptoms: chills and fever, head-ache, dizziness
Fatigue
Flushing
No relevant changes in routine laboratory values
No SAEs nor Grade 3/4 toxicities

Adeno-IFN-γ before
before
after 1st injection
after 2nd injection

P-M 009
## Outcome/Response

### OR: 11/20  3/12  8/17

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>DG</th>
<th>Stage</th>
<th>Dose (tp)</th>
<th>No. of injections</th>
<th>Response I.L.</th>
<th>Response non I.L.</th>
<th>Response overall</th>
<th>Response duration</th>
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<td>MF</td>
<td>Ib</td>
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<td>CR</td>
<td>CR</td>
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<td>CR</td>
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<td>CR</td>
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</table>
PUVA resistant CD30+ CTCL

3 months later

9 months later
Mycosis fungoides

before

after 9 injections
Primer design for vector encoded vs. endogenous IFN-\(\gamma\)

- TG1042-derived IFN-\(\gamma\) primers
- Endogenous IFN-\(\gamma\) primers
TG1042-derived IFN-γ and endogenous IFN-γ
TG1042-derived IFN-γ and endogenous IFN-γ
Mycosis fungoides

before

H&E

after

H&E
Mycosis fungoides

before

after

TIA

TIA
CBCL

before
Injections

after 3 Injections

H&E

H&E