ACRレポート2008

10月24日～29日，San Francisco

京都大学大学院医学研究科　内科学講座臨床免疫学
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2008年の演題数

- Plenary session: 2演題
- Current Abstract Session: 17演題
- Poster Session: 135演題（日本から11演題）

Plenary SessionI
（638）Fra2-Tg mouse

- Fra2: AP-1ファミリーに属する転写因子
  PDGFがFra2の発現を促す
- Transgenic mouse
  fibrosis (肺，皮膚)，肺動脈の閉塞
  TUNEL/Caspase (+)細胞が増加
  血管内皮にFra2 siRNA→血管形成改善
  自己抗体形成は無かった.
- ヒトSScの皮膚でもFra2の発現増加

Plenary SessionI
（639）Tadarafil for Raynaud’s phenomenon (RP)

- PDE5 阻害薬（sildenafilより半減期が長い）
- RP＋指尖潰瘍例にTadarafil or Placebo 6 week
  → washout →症例を入れ替えて6 week （全24症例）
- 結果（Baseline/ Placebo / Tadarafil）
  daily duration (時間): 3.4 / 3.3 / 2.2
  投与前後の潰瘍指の総計 Placebo 13→10
  Tadarafil 24→0

・Adverse effectに明確な差は無かった.

Clinical Symposium: The great debate
CyclophosphamideはSScの病態を改善させるか？

1) Do you believe that CY is an effective therapy for SSc lung disease after it is stopped?
   Y: 60% N: 40%
2) Do you believe that CY is an effective Tx for extra-pulmonary SSc in the long term (greater than 2 years) ?
   Y: 22% N: 78%
3) Is CY's risk/ benefit profile in SSc acceptable or not in the long term (greater than 2 years) ?
   Y: 45% N: 55%
4) Should CY be considered a "disease modifying" agent in scleroderma?
   Y: 55% N: 45%

Clinical Symposium: The great debate
CyclophosphamideはSScの病態を改善させるか？

Pro perspective and discussion--- Daniel E. Furst; UCLA

1) Yes. (Lung)
   SLS study→%FVCの変化が有意に改善.
2) Yes. (extrapulmonary)
   For function, QOL and Skin score
3) Yes. (risk/benefit)
   SLS studyでは, severe AEに明らかな差は無かった.
   長期使用による副作用の頻度は不明.
4) Yes. (disease modifying drug?)
   Ann Intern Med: alveolitis→CY使用群で生命予後改善.

Clinical Symposium: The great debate
CyclophosphamideはSScの病態を改善させるか？

Con perspective and discussion---James R. Seibold; Univ. of Michigan

Nannini C et al. (ART 2008)

Based on available data (380 subjects), CY DOES NOT appear to result in clinically significant improvement of pulmonary function.

(SLEで)CY使用による子宮頸癌の発症率が有意に増加.

Should CY be used? …..MAYBE SOMETIMES

Clinical Symposium: The great debate
CyclophosphamideはSScの病態を改善させるか？

1) Do you believe that CY is an effective therapy for SSc lung disease after it is stopped?
   Y: 60% N: 40% → Y: 53% N: 47%
2) Do you believe that CY is an effective Tx for extra-pulmonary SSc in the long term (greater than 2 years) ?
   Y: 22% N: 78% → Y: 33% N: 67%
3) Is CY's risk/ benefit profile in SSc acceptable or not in the long term (greater than 2 years) ?
   Y: 45% N: 55% → Y: 50% N: 50%
4) Should CY be considered a "disease modifying" agent in scleroderma?
   Y: 55% N: 45% → Y: 48% N: 52%

Concurrent Abstract Session
（1221）Imatinibの治療実験

- Imatinib mesylate (IM, Gleevec): selective tyrosine kinase inhibitor (Abl and PDGF)
- Bleomycin誘導性皮膚硬化に対する予防実験はすでに報告あり→一旦生じた線維化を修復する効果はあるのか？
- Model for treatment of pre-established fibros: local injections of bleomycin every other day.
- Bleomycin injection前との，skin thicknessの変化：

  3w Ble. →148 ± 14%

  3w Ble. + 3w Ble. →168 ± 10%

  3w Ble. + (3w Ble. + IM 150mg/kg/d) →124 ± 12%

  (上記2者どちらの比較とも$p < 0.05$)

Concurrent Abstract Session
（1222）Imatinib: Phase IIa Trial（中間報告）

Single center, Open label, IM 400mg/d for diffuse SSc

Target recruitment　20 Pts with < 4 years of disease
10 Pts with 4 to 10 years

evaluation : histories, physical exam., SF-36s, sHAQs, Lab data, skin biopsies, chest X-ray, PFTs, ECG, mRSS

- 18 例で治療開始.
- 3M後の評価が10例で，6M後の評価が5例で可能であった.
- 15例にAEを認めた；CK elevations (n=7), edema (n=7), nausea (n=7)
- 2例にsevere AEを認めたが，いずれもIMとの関連性は否定的であった.

Change in mRSS.

Patient Id	Disease Duration	Total time on Gleevec	Baseline mRSS	Month 3 mRSS	Month 6 mRSS
G1	1.5 years	7 months	21	26	28
G2	3 years	7 months	30	29	27
G3	<4 years	3 months	26	20	24
G4	<3 years	7 months	24	24	24
G5	6 years	6 months	20	15	10
G6	<1 year	5 months	43	40	
G7	7 years	1 month	31	27	
G8	<1 year	3 months	25	21	
G9	3.5 years	3 months	46	45	
G10	<1 year	3 months	41	46	
MEAN (S.D.) at 3 months (G1 – G10)			30.7 (9.4)	29.3 (10.8)	
MEAN (S.D.) at 6 months (G1 – G5)			24.2 (4.0)	22.8 (5.4)	22.6 (7.3)

(Abstractより改変)

Conclusion: Imatinibは，安全性・認容性のある
SScの治療薬として期待される.

Concurrent Abstract Session
（1223）Autologous stem cell transplantation

- Update on ASTIS-trial
- High dose immunosuppressive therapy (HDIT) + hematopoietic stem cell transplantation (HSCT)
- 移植群: Mobilization with CY 2×2 g/m2, conditioning with CY 200 mg/kg, rbATG 7.5 mg/kg, followed by reinfusion of CD34+ selected autologous HSCT
- 対照群:12x monthly i.v. bolus CY 750 mg/m2
- Primary endpoint = event free survival during 2 years follow-up.

Concurrent Abstract Session
（1223）Autologous stem cell transplantation

Results

- 2008年4月で，10カ国25施設118症例がenrolled.
- Mean disease duration: 1.8 yr.
- 6 か月目のfollowとして，91例(43:移植群，48：対照群)の安全性情報を回収.
- 平均29か月(1-72)の観察で，Grade 3 or 4の毒性は移植群15例（/43），対照群13例(/48）で認められた→両群間に有意差は認められず.

Concurrent Abstract Session
（1225）Bosentan (TRUST 3-year data)

- 53 例のPAH-CTD (WHO Functional Class Ⅲ)
  (42 例: SSc, 5例: SLE, 6例: Overlap CTD)
- ボセンタン投与量 4 週間: 62.5mg twice a day
  →44週間: 125mg twice a day
- Kaplan-Meier法を用いた生存率
  1年目：92.3％→2年目：78.7％→3年目：69.9％
- Functional Class の改善を認めた症例：55.9％
  （95%CI: 37.9 – 72.8）