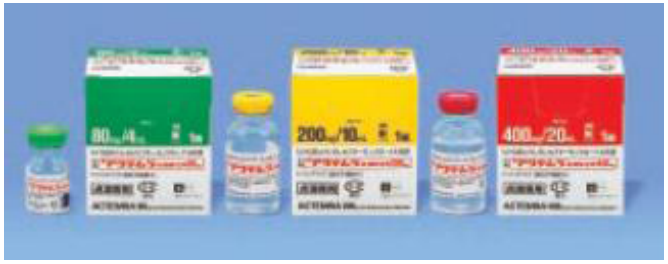
CHUGAI
Roche Roche Group

Actemra®
tocilizumab

Product Overview of Actemra



日本標準商品分類番号 87639

ヒト化抗ヒト IL-6 レセプターモノクローナル抗体
生物由来製品、劇薬、指定医薬品、処方せん医薬品注)

薬価基準収載
アクテムラ®点滴静注用200mg
Actemra® トシリズマブ(遺伝子組換え)注
tocilizumab
効能追加

薬価基準未収載
アクテムラ®点滴静注用80mg 400mg
Actemra® トシリズマブ(遺伝子組換え)注
tocilizumab
近日発売

注)注意－医師等の処方せんにより使用すること

CHUGAI PHARMACEUTICAL CO.,LTD.
Actemra Product Manager
Tadao Shimizu

2008.05.22

Forward-Looking Statements

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the "Company"). These statements reflect the Company's current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company's businesses.

Major Biologics for Rheumatoid Arthritis (RA)

Type			Generic Name (Brand Name)	Japan	Overseas
Drugs targeting cytokines or their receptors	TNF inhibitor	Chimeric anti-TNF-α antibody	infliximab (Remicade)	Approved	Approved
		Human anti-TNF- α antibody	adalimumab (Humira)	Approved	Approved
		TNF receptor-Fc fusion protein	etanercept (Enbrel)	Approved	Approved
		Human anti-TNF- α antibody	Golimumab	Under development	Under development
	IL-6 inhibitor	Humanized anti-IL-6 receptor antibody	tocilizumab (Actemra)	Approved	Filed
	IL-1 inhibitor	IL-1 receptor antagonist	anakinra (Kineret)	-	Approved
Drugs targeting functional molecules on cellular surface	B-cell inhibitor	Chimeric anti-CD20 antibody	rituximab (Rituxan)	-	Approved
		Humanized anti-CD20 antibody	ocrelizumab	Under development	Under development
	T-cell inhibitor	CTLA-4-Fc fusion protein	abatacept (Orencia)	Under development	Approved

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History of Development

- 1986 Cloning of IL-6 (Osaka University, Kishimoto and others)
  Joint development started with Osaka University
- 1988 Cloning of IL-6 receptor
- 1990 gp130 structure elucidation
- 1997 Initiation of clinical development for RA
- 2001 Initiation of clinical development for Castleman's disease
- 2002 Initiation of clinical trial for systemic juvenile idiopathic arthritis (sJIA)
- 2003 License agreement of MRA with Roche
- 2005 Approval for indication of Castleman's disease in Japan
- 2006 Application for additional indications of RA and JIA
- 2007 Biological License Application for RA in the US and Europe
- 2008 Approval in Japan for additional indications of RA, polyarticular-course JIA and sJIA

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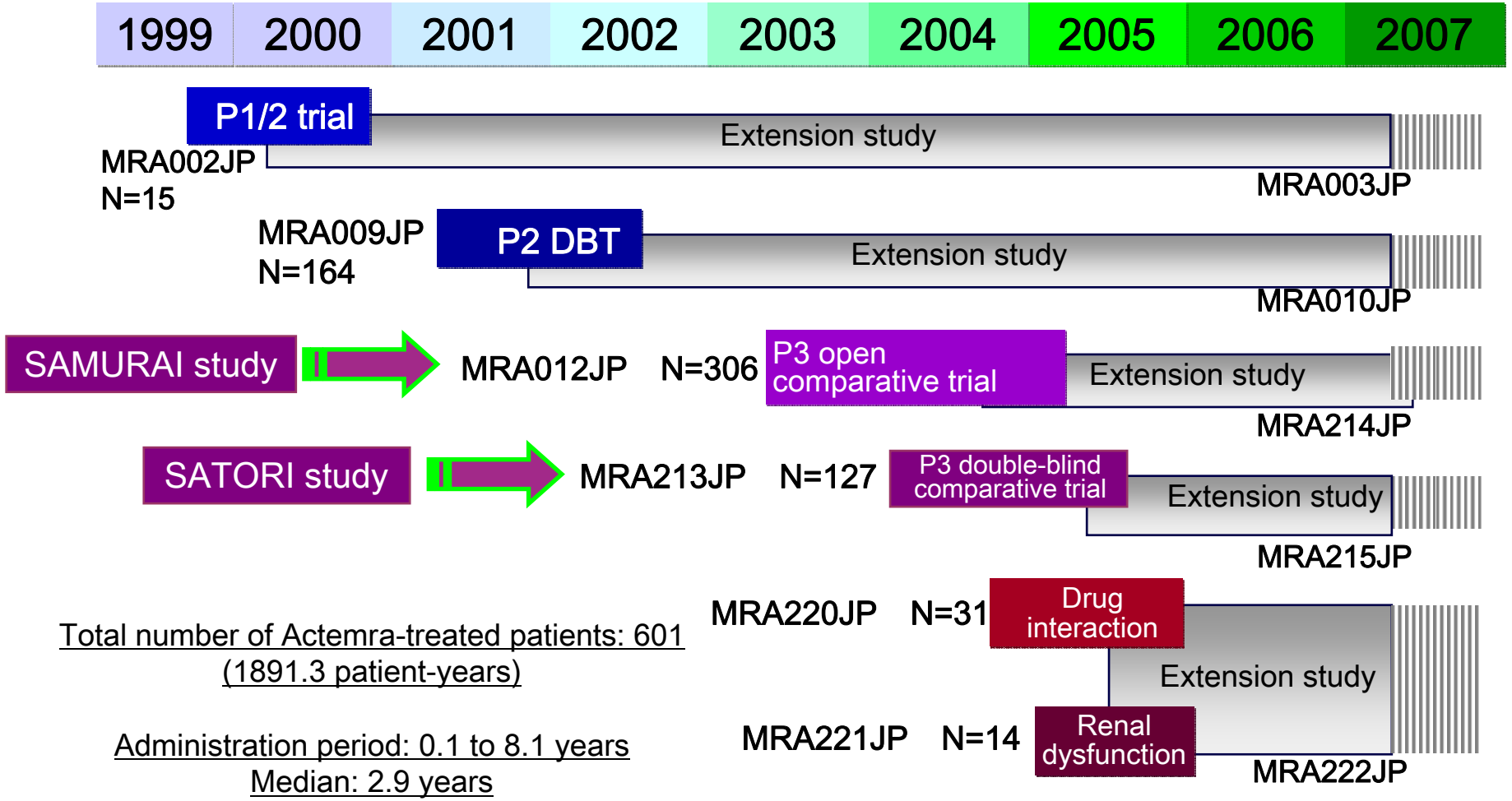
Overview of Clinical Studies Conducted in Japan (RA)



Total number of Actemra-treated patients: 601
(1891.3 patient-years)

Administration period: 0.1 to 8.1 years
Median: 2.9 years

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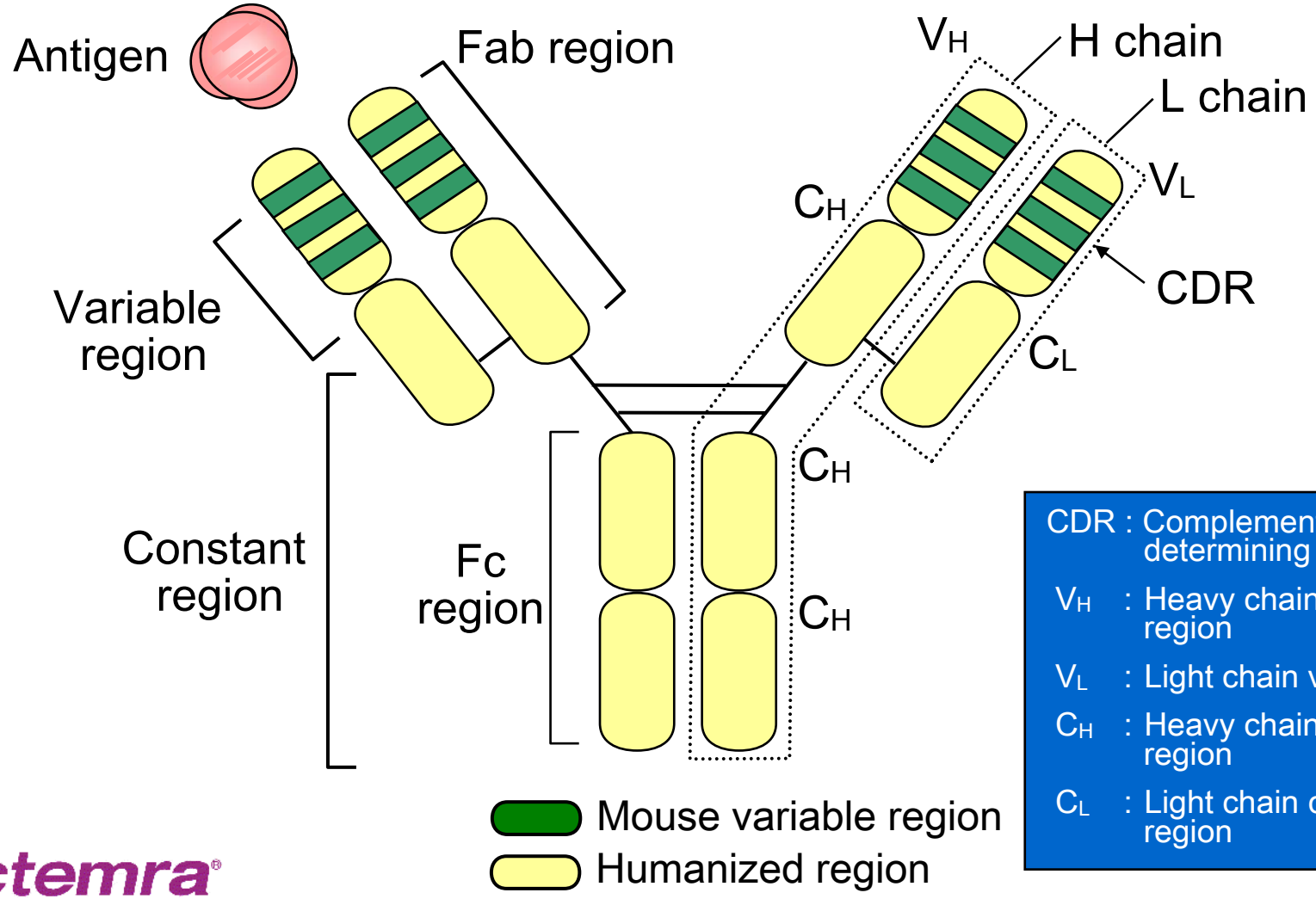
* Extension studies were conducted for every trial in Japan

Structure of Actemra



CDR : Complementary determining region

V_H : Heavy chain variable region

V_L : Light chain variable region

C_H : Heavy chain constant region

C_L : Light chain constant region

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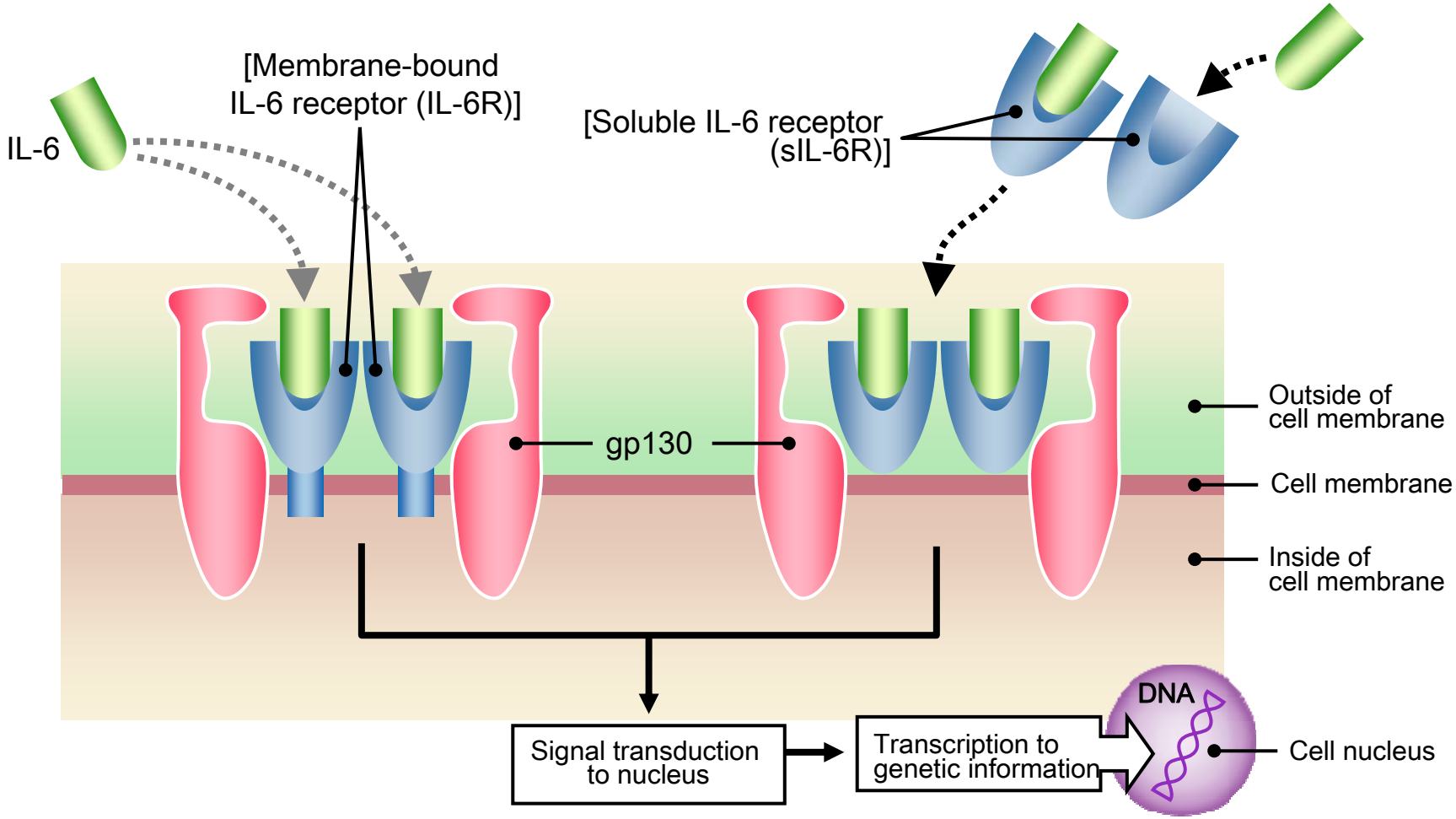
Signal Transduction by IL-6



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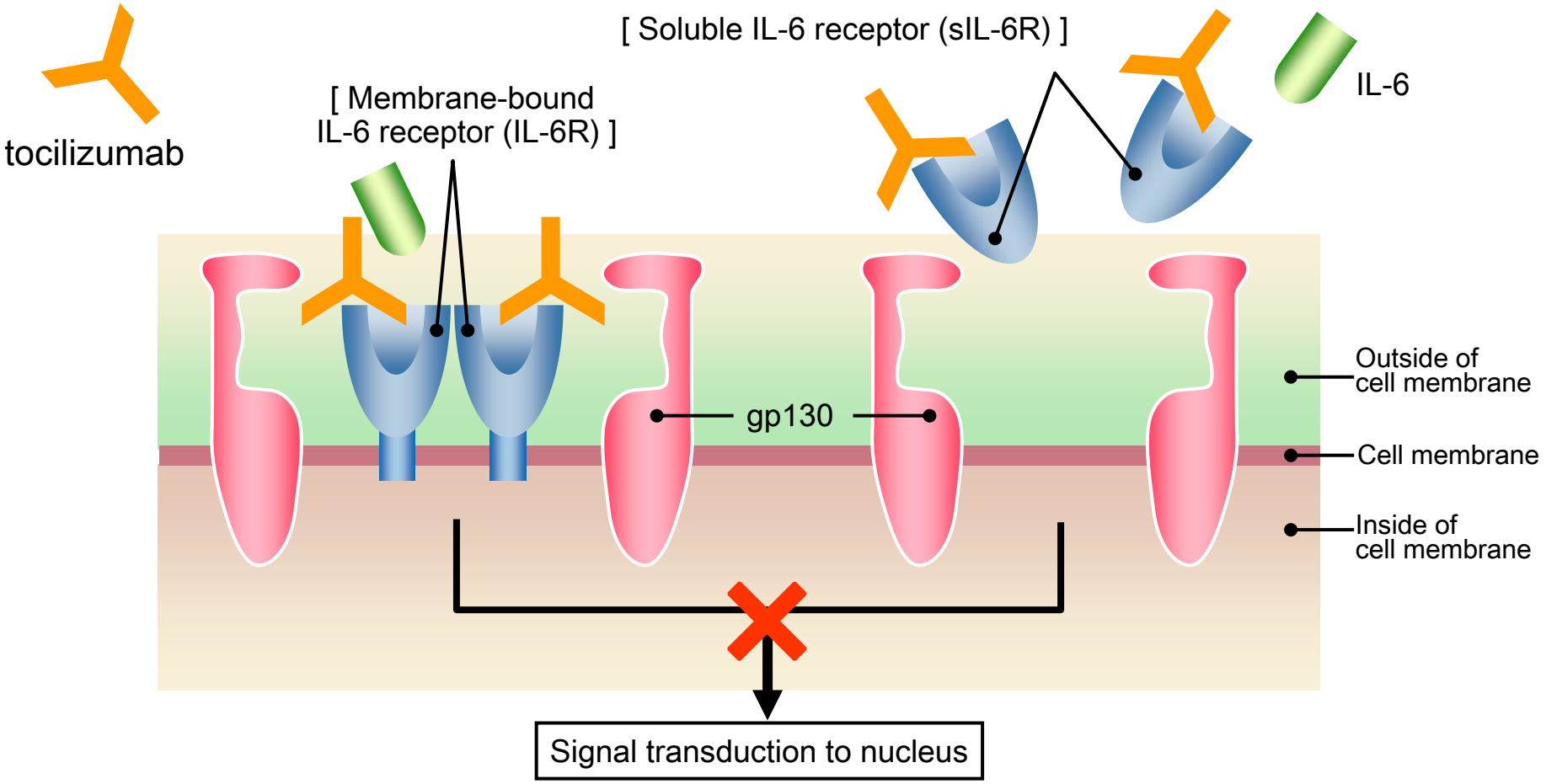
Inhibition of Signal Transduction of IL-6 by Actemra



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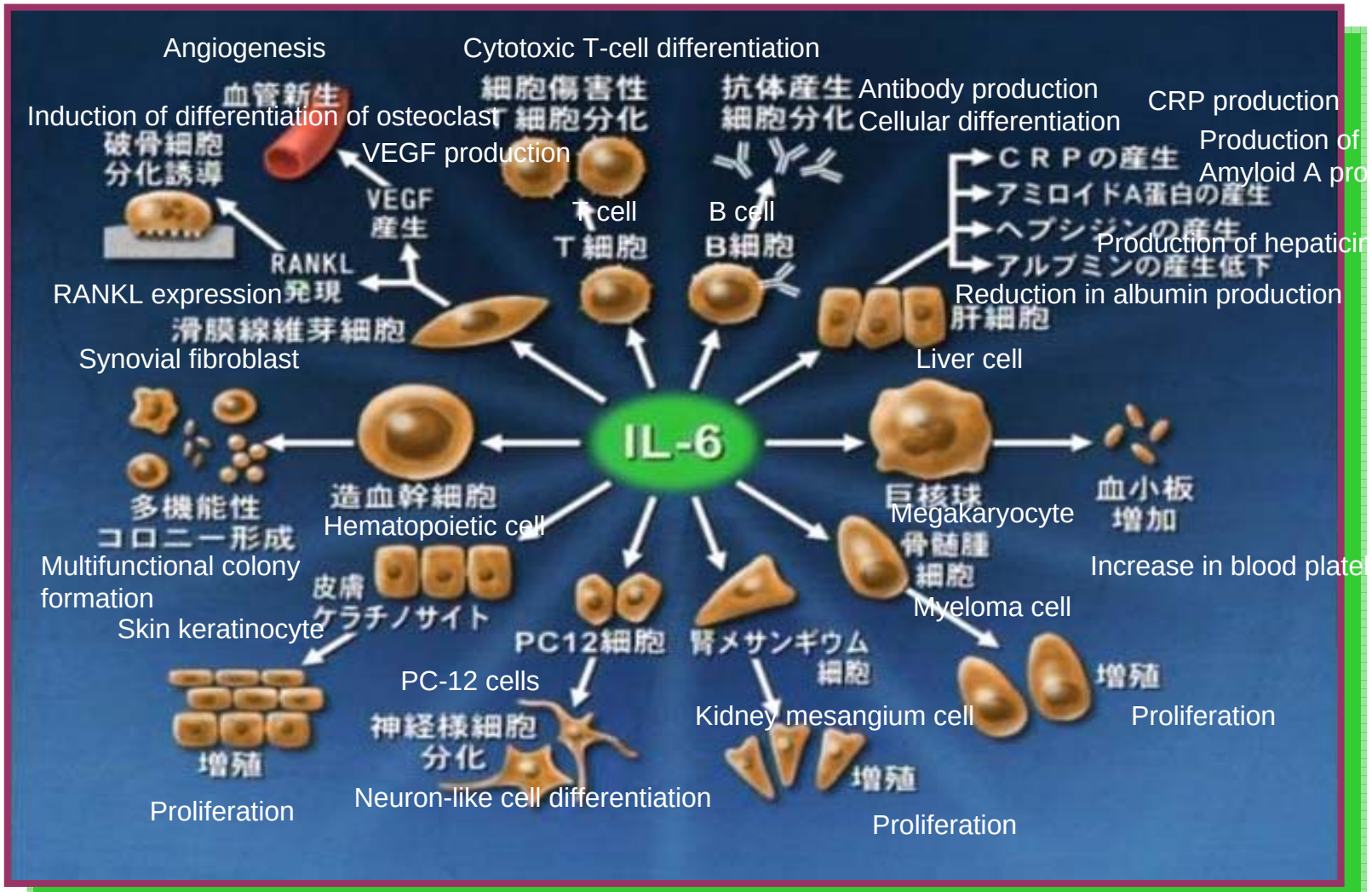
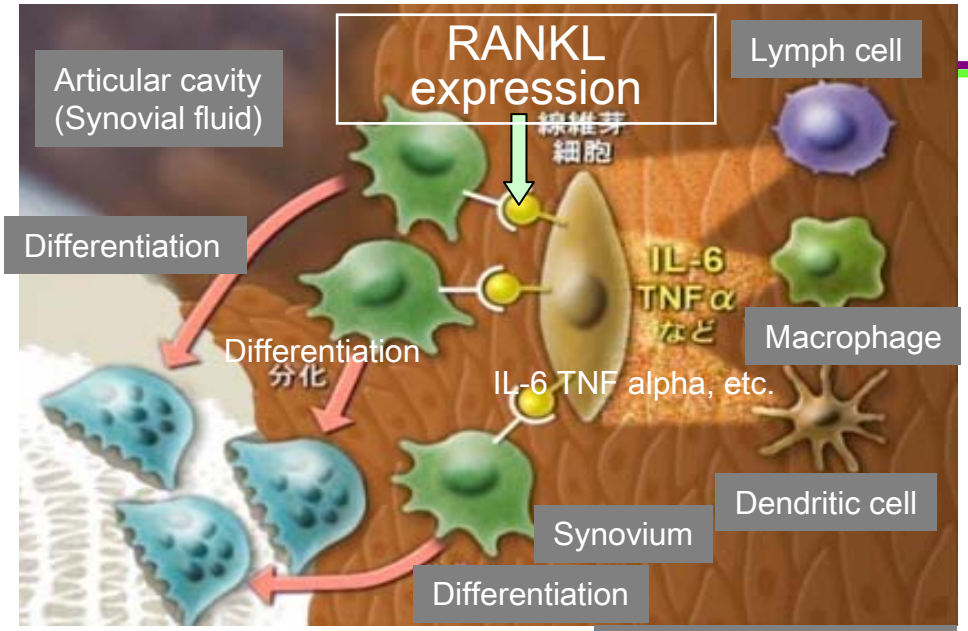
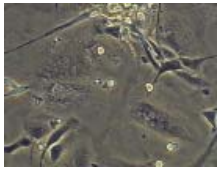
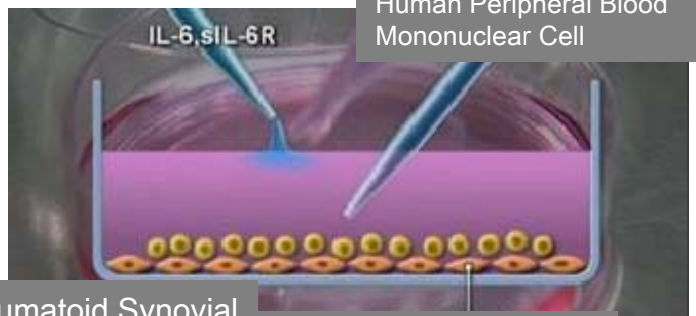
Biological Activities of Interleukin-6 (IL-6)



Activities of Actemra on Suppression of Osteoclastic Cell Formation







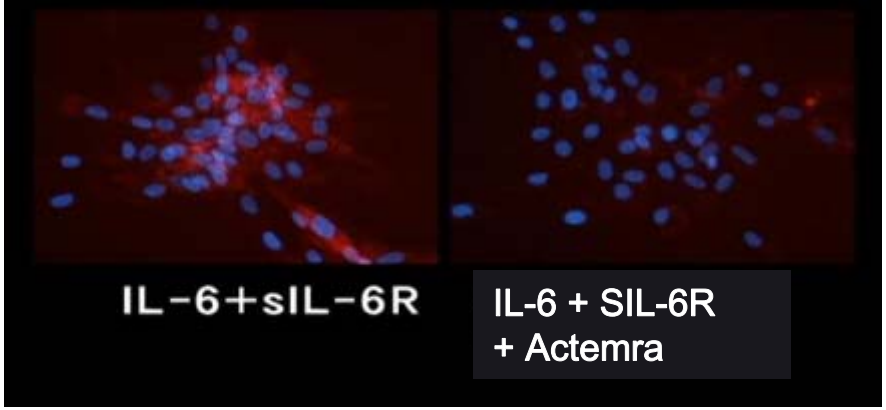
Human Peripheral Blood Mononuclear Cell

Rheumatoid Synovial Fibroblasts

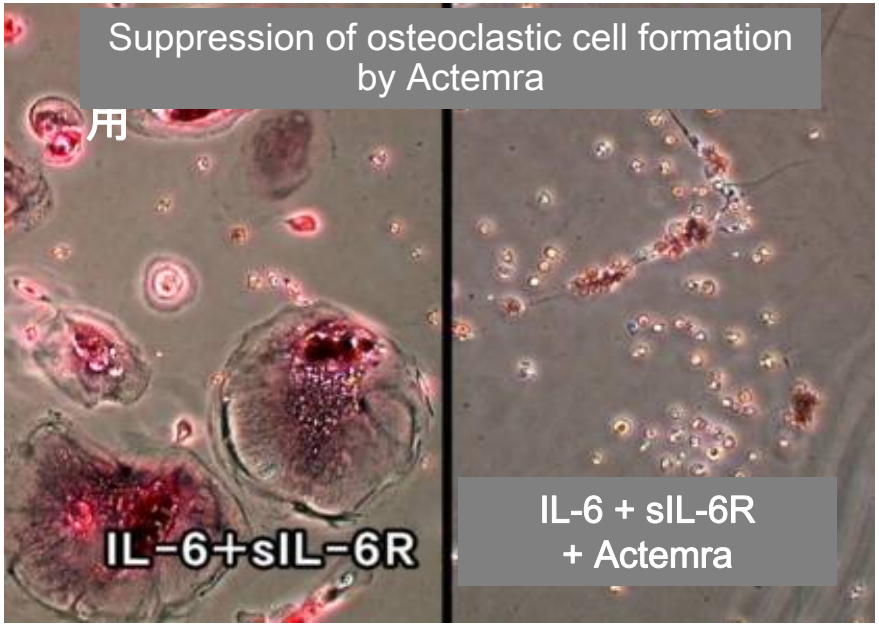
Rheumatoid Arthiritis

Actemra suppresses synovial cell formation through its action of suppressing RANKL expression by synovial fibroblasts. (in vitro)

Suppression of RANKL expression by Actemra



Suppression of osteoclastic cell formation by Actemra



Indications

- The following diseases which do not show sufficient response to the existing therapies

  - Rheumatoid arthritis[1)]
    (including inhibition of progression of structural joint damage)
  - Polyarticular-course juvenile idiopathic arthritis [1)]
  - Systemic juvenile idiopathic arthritis[2)]

1) Actemra should be administered to patients who have failed to show sufficient response in the past despite receiving appropriate treatment with one or more anti-rheumatic drugs.
2) Actemra should be administered to patients who have failed to show sufficient response in the past despite receiving appropriate treatment with corticosteroids.

Dosage and Administration

- RA and polyarticular-course JIA

  The recommended dose of tocilizumab (genetical recombination) is 8mg/kg as a single intravenous drip infusion administered at 4-week intervals.

- Systemic JIA and Castleman's disease

  The recommended dose of tocilizumab (genetical recombination) is 8mg/kg as a single intravenous drip infusion administered at 2-week intervals.

  The dosing interval can be shortened to a minimum of 1 week depending on the patient's disease condition.

Safety

Out of 783 cases, adverse events were reported in 751 cases (95.9%)

- Major adverse events
  - Nasopharyngitis 421 cases (53.8%)
  - Cholesterol increased 292 cases (37.3%)
  - LDL increased 148 cases (18.9%)
  - Triglycerides increased 126 cases (16.1%)
  - ALT(GPT) increased 119 cases (15.2%)

- Serious adverse events
  - Infection, anaphylactic shock, anaphylactoid symptoms, digestive tract rupture, neutropenia, heart failure

※Breakdown of 783 cases: Castleman's disease--35 cases; RA--601 cases; polyarticular-course JIA--19 cases; sJIA--128 cases.

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Product Characteristics

1．Actemra is an original product from Japan and the first humanized anti-IL-6 receptor monoclonal antibody in the world.

2．Rheumatoid arthritis

- Demonstrated high efficacy by monotherapy in active RA patients taking methotrexate. (24 weeks Japanese phase III clinical study: SATORI study)
- Demonstrated high efficacy by monotherapy in RA patients who had inadequate response to DMARDs. (52 weeks Japanese phase III clinical study: SAMURAI study)
- Improved anemia, serum amyloidosis and laboratory parameters of MMP-3.

3．To demonstrate significant efficacy in polyarticular-course juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis. (Japanese phase III clinical studies)

Conditions for Approval
- Post-Marketing Surveillance -

For RA, polyarticular-course JIA, systemic JIA

1. In post-marketing, until data is gathered for a fixed number of patients, safety and efficacy data for Actemra should be collected by conducting a drug use-results survey of all cases and necessary measures should be taken for the proper use of Actemra.

2. A large-scale post-marketing surveillance should be conducted with a comprehensive investigation of the safety of Actemra including the safety of long-term treatment and occurrence of infections, etc.

Website


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