

GLADAR

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# RHEUMATOID ARTHRITIS IN LATIN AMERICA

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# GLADAR

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## MOTIVATION BASED ON :

- *Shortage of epidemiologic information*
- *Necessity of quality- quantification of the Latin American reality of RA*

LA own characteristics

Demographics  
Socio-economics  
Environments

# GLADAR

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graph TD; A[GLADAR] --> B[L-A Consensus Meeting on RA]; A --> C[Epidemiological Study (Cohort)]; B --> D[1st Consensus Quito (Sep/03)];
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**L-A Consensus  
Meeting on RA**

**1st Consensus  
Quito (Sep/03)**

**Epidemiological  
Study (Cohort)**

# 1° L-A Consensus of RA Treatments (Quito, Sep/03)



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## First Latin-American Consensus of RA Treatments (Quito, Sep/03)

### **OBJECTIVES**

To develop a consensus document that may unify and guide the pharmacological management of RA in Latin America and the Caribbean

A secondary objective was the diffusion of the consensus conclusions and recommendations in participating countries

# RHEUMATOLOGY

VOLUME 45 SUPPLEMENT 2 JUNE 2006

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List of participants

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First Latin American position paper on the pharmacological treatment of  
rheumatoid arthritis

*By the Latin American Rheumatology Associations of the Pan-American  
League of Associations for Rheumatology (PANLAR) and the Grupo  
Latinoamericano de Estudio de Artritis Reumatoide (GLADAR)*

ii7

## PANAMA

### Sociedad Panameña de Reumatología

*Ángel F. Achurra*

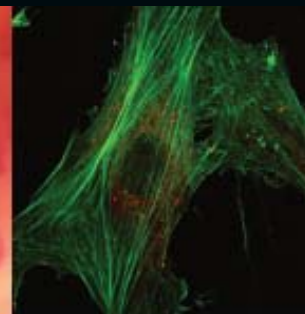
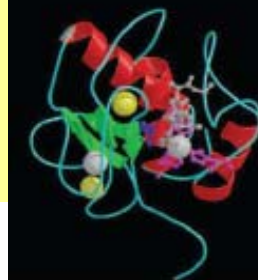
Complejo Hospitalario Metropolitano de la Caja de Seguro Social  
Dr. Arnulfo Arias Madrid. Facultad de Medicina de la  
Universidad de Panamá. Ciudad de Panamá.

## PARAGUAY

### Sociedad Paraguaya de Reumatología

*Ernesto Paredes Domínguez*

Hospital de Clínicas de la Facultad de Medicina.  
Universidad Nacional de Asunción. Asunción.



# RHEUMATOLOGY

VOLUME 45 SUPPLEMENT 2 JUNE 2006

[www.rheumatology.oxfordjournals.org](http://www.rheumatology.oxfordjournals.org)

## FIRST LATIN AMERICAN POSITION PAPER ON THE PHARMACOLOGICAL TREATMENT OF RHEUMATOID ARTHRITIS

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### Country

Argentina  
Brasil  
Chile  
Colombia  
Costa Rica  
Cuba  
Ecuador  
Guatemala  
México  
Nicaragua  
Panamá  
Paraguay  
Perú  
Republica Dominicana  
Uruguay  
Venezuela

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### Participating Societies

Sociedad Argentina de Reumatología  
Sociedade Brasileira de Reumatología  
Sociedad Chilena de Reumatología  
Asociación Colombiana de Reumatología  
Asociación Costarricense de Reumatología  
Sociedad Cubana de Reumatología  
Sociedad Ecuatoriana de Reumatología  
Asociación Guatemalteca de Reumatología  
Colegio Mexicano de Reumatología  
Asociación Nicaragüense de Reumatología  
Sociedad Panameña de Reumatología  
Sociedad Paraguaya de Reumatología  
Sociedad Peruana de Reumatología  
Sociedad Dominicana de Reumatología Inc.  
Sociedad Uruguaya de Reumatología  
Sociedad Venezolana de Reumatología

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**L-A Consensus Meeting on RA**

**1st Consensus Quito (Sep/03)**

**2nd Consensus Reñaca (Oct/05)**

**Epidemiological Study (Cohort)**



Pan American League Of  
Associations For Rheumatology

GLADAR  
Grupo Latino Americano De estudio de Artritis Reumatoide

*Reñaca - Chile, 2005*

Leading role as coordinators	Subjects	
	Education	Therapy
<b>María Eugenia Suárez Almazor (USA)</b>	<b>Patient education (1)</b> <ol style="list-style-type: none"> <li>1. <b>María E. Suárez-Almazor</b></li> <li>2. Julio Hofman (Argentina)</li> <li>3. Manoel Bertolo (Brasil)</li> <li>4. Mario Moreno (Ecuador)</li> <li>5. <b>Angel Achurra (Panamá)</b></li> <li>6. Evelyn Hess (Estados Unidos)</li> <li>7. Napoleón Peña (Venezuela)</li> </ol>	<b>Drug safety surveillance (5)</b> <ol style="list-style-type: none"> <li>1. <b>Roger Levy (Brasil)</b></li> <li>2. Francisco Caeiro (Argentina)</li> <li>3. William Otero (Colombia)</li> <li>4. Rubén Montufar (El Salvador)</li> <li>5. Margarita Duarte (Paraguay)</li> <li>6. Jaime Hernández (Uruguay)</li> <li>7. Héctor Gatica (Chile)</li> </ol>
<b>Mario Cardiel (México)</b>	<b>Community education (2)</b> <ol style="list-style-type: none"> <li>1. <b>Carlo Vinicio Caballero (Colombia)</b></li> <li>2. Horacio Venarotti (Argentina)</li> <li>3. Pedro Miranda (Chile)</li> <li>4. Osvaldo Caliste (Cuba)</li> <li>5. Nilmo Chávez (Guatemala)</li> <li>6. Juan Angulo (Perú)</li> <li>7. Kate Lorig (Estados Unidos)</li> </ol>	<b>Indications of biologics for incomplete responders to classic DMARDs (6)</b> <ol style="list-style-type: none"> <li>1. <b>Alberto Millán (Venezuela)</b></li> <li>2. Pablo Riedemann (Chile)</li> <li>3. Rafael Valle (Colombia)</li> <li>4. Francisco Girón (Honduras)</li> <li>5. Armando Calvo (Perú)</li> <li>6. Boulos Haroui (Canadá)</li> <li>7. Sergio Jacobelli (Chile)</li> </ol>
<b>Bernardo Pons-Estel (Argentina)</b>	<b>Health policy and decisions (4)</b> <ol style="list-style-type: none"> <li>1. <b>Enrique Soriano (Argentina)</b></li> <li>2. Sebastian Radominski (Brasil)</li> <li>3. Loreto Massardo (Chile)</li> <li>4. Oscar Uribe (Colombia)</li> <li>5. Marlene Guibert (Cuba)</li> <li>6. José A. Herrera (Venezuela)</li> <li>7. Adriana Silvestre (Argentina)</li> </ol>	<b>Programs for early detection and appropriate treatment of RA (7)</b> <ol style="list-style-type: none"> <li>1. <b>Eduardo Acevedo (Perú)</b></li> <li>2. Luis José Catoggio (Argentina)</li> <li>3. Fernando Cavalcanti (Brasil)</li> <li>4. Miguel Gutiérrez (Chile)</li> <li>5. Renato Guzmán (Colombia)</li> <li>6. Leonor Barile (México)</li> <li>7. Alicia Ramagli (Uruguay)</li> </ol>
<b>Carlos Pineda (México)</b>	<b>Other health professionals educ.</b> <ol style="list-style-type: none"> <li>1. <b>Ieda Laurindo (Brasil)</b></li> <li>2. María Luisa Gil (Bolivia)</li> <li>3. Carlos Fuentealba (Chile)</li> <li>4. Ricardo Sáenz (Costa Rica)</li> <li>5. Francisco Rosas (México)</li> <li>6. Rafael Alba Féris (Rep. Dominicana)</li> <li>7. Sergio Aragón (Nicaragua)</li> </ol>	<b>The role of classic DMARDs (8)</b> <ol style="list-style-type: none"> <li>1. <b>Rolando Espinosa (México)</b></li> <li>2. John Londoño (Colombia)</li> <li>3. Licia da Mota (Brasil)</li> <li>4. Nilzio Antonio da Silva (Brasil)</li> <li>5. Claudio Galarza (Ecuador)</li> <li>6. Arnulfo Nava (México)</li> <li>7. Alfredo Sánchez (Perú)</li> </ol>

# GLADAR

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**L-A Consensus Meeting on RA**

**1st Consensus Quito (Sep/03)**

**2nd Consensus Reñaca (Oct/05)**

**Epidemiological Study (Cohort)**

**1st Investigator Rio (Dec/03)**

**2nd Investigator Rio (May/06)**

**Latin-American cohort of patients  
with early rheumatoid arthritis (ERA)**

**GLADAR**

***GRUPO LATINOAMERICANO DE ESTUDIO DE  
ARTRITIS REUMATOIDEA***

# GLADAR COHORT

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## *Design of the Study*

Prospective, observational, multicenter,  
multinational inception cohort

# GLADAR COHORT

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## *Objectives*

Evaluating the potential influences of ethnic, social and demographic variables on:

- Clinical characteristics
- Treatment patterns
- Outcomes

of early RA in patients from Latin America

# GLADAR COHORT

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## *Centers and patients selection*

- 14 Latin-American countries
- 46 centers selected on demonstrated expertise in RA
- Number of centers was selected in proportion to the population of each country
- Balanced representation of the initial cohort (minimum of 20 and a maximum of 30 consecutive patients)

COUNTRIES	Population (per million)
Argentina	38
<b>Bolivia</b>	<b>9</b>
Brazil	172
Chile	15
Colombia	43
Costa Rica	4
Cuba	10
Dominican (Rep)	9
Ecuador	13
El Salvador	1
<b>Guatemala</b>	<b>12</b>
<b>Honduras</b>	<b>7</b>
México	99
<b>Nicaragua</b>	<b>5</b>
Panama	3
<b>Paraguay</b>	<b>6</b>
Peru	26
Uruguay	3
Venezuela	25



# GLADAR COHORT

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## *Inclusion criteria*

- 18 years or older
- < 1 year of disease onset
- Diagnosis based on ACR core criteria
- A maximum of 25% of patients with as few as 3 of the ACR criteria (high confidence in a diagnosis of RA)
- $\geq 50\%$  patients DMARD-naïve at the time of enrollment

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## *Material and Methods*

### Evaluations

- **Clinical / laboratory:** BL, 3, 6, 12, 18, 24 months

#### Instruments

- DAS28
- Visual analog scale
- HAQ
- SF-36

- **X-ray: hands / feet:** BL, 12 and 24 months

**Data base**

ARTHROS 6.1

# GLADAR COHORT (Analysis 31-Mar-06)

Countries	Centers	Patients
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Argentina	5	140
Brazil	12	261
Chile	2	61
Colombia	5	115
Costa Rica	1	23
Cuba	1	35
Dominican Rep.	1	23
Ecuador	2	51
El Salvador	1	30
México	8	172
Panama	1	8
Peru	3	65
Uruguay	1	22
Venezuela	3	87

<b>Total: 14</b>	<b>46</b>	<b>1.093</b>
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# GLADAR COHORT

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## *Demographic data*

### 4 Major ethnics groups (N: 1.059)

	N	%
• Mestizos	473	43
• Caucasians	343	31
• ALA	204	19
• Amerindians	39	4

# GLADAR COHORT

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## *Demographic data*

<b>Cohort</b>	<b>GENDER</b>				<b>RATIO F : M</b>
	<b>Female</b>		<b>Male</b>		
	n	%	n	%	
GLADAR (ERA)	930	85	163	15	6 : 1
GEN-AR (Sep 2006)	1606	85	283	15	6 : 1
Literature	-	-	-	-	2 - 4 : 1

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## *Distribution by gender & ethnic groups*

<b>Ethnic groups</b>	<b>Gender</b>	<b>Patients</b>		<b>F:M Ratio</b>	<b>p</b>
Total	F	930	85%	6 : 1	0.476
	M	163	15%		
Caucasians	F	287	84%	5 : 1	
	M	56	16%		
ALA	F	173	85%	6 : 1	
	M	31	15%		
Mestizos	F	407	86%	6 : 1	
	M	66	14%		
Amerindians	F	36	92%	12 : 1	
	M	3	8%		

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## *Demographic data*

### Formal Education

$\leq 10$  y — 59 %  
Illiterate — 22 %

### Socioeconomic Status (M. Graffar)

Lower Middle / Lower — 58 %

### Medical Coverage

Partial or no coverage — 44 %

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## *Epidemiologic data*

	Mean	SD	Min - Max
• Age at onset (y)	<b>46.0</b>	±14.2	18 - 85
• Age at diagnosis (y)	<b>46.5</b>	±14.2	19 - 86
• Disease duration (1 <sup>o</sup> v) (m)	<b>5.8</b>	±3.8	1 - 26
• Follow up (m)	<b>15.6</b>	±7.3	1 - 39

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## *Demographic data*

### Gender - Age at disease onset (mean)

	years	SD	p
Female	45	±14.2	< 0.001
Male	50	±13.9	

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## *Demographic data*

### Ethnic Groups - Age at disease onset (mean)

	years	SD	p
Amerindians	44	±14.8	
ALA	45	±13.5	< 0.001
Mestizos	45	±13.6	
Caucasians	49	±15.1	

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## ***Clinical Manifestations (cumulative)***      %

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• Symmetric polyarthritis	95
Insidious onset	68
Additive course	93
• Morning stiffness ( $\geq 1$ h)	88
• Fatigue	43
• Sicca syndrome	14
• Fever	12
• Bone / joint deformities	11
• Myalgias	11
• Rheumatoid nodules	6
• Infections (any)	5
• Extra-articular manifestations	12

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## *Laboratory & Radiology* %

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### HEMATOLOGY

Anemia	45
Leucocytosis	32
Thrombocytosis	22

### IMMUNOLOGY

RF (+)	76
ANA (+)	27

### RADIOLOGY

ACR X-ray changes	32
Joint erosions	25

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## *Treatment Patterns (cumulative)*

<b>Drug</b>	<b># Pt</b>	<b>%</b>	<b>CI (%)</b>
<b>NSAIDs</b>	946	86	84 - 88
<b>Corticosteroids</b>	806	74	71 - 76
Pred. ≤10 mg	618	77	74 - 80
Pred. ≥20 mg	44	6	4 - 7
IV pulse	12	1	0.5 - 1.9
IA injections	12	5	4 - 7
<b>DMARDs</b>	1,001	92	90 - 93
<b>Biologics</b>	46	4	3 - 6

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## *DMARDs (I)*

	<b># Pts</b>	<b>%</b>
• DMARDs	1,001	92
• DMARDs-naïve (at enrollment)	858 *	79
• DMARDs (initiated the 1st month after initial visit)	474	43

\* 858/1083

Disease duration without DMARDs

6.8 months (SD  $\pm$  4.4)

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## *DMARDs ( II )*

	# Pts	%
• <b>DMARDs</b>	1,001	92
Metotrexate (MTX)		82
Antimalarials (CQ/HCQ)		46
Sulfazalazine (SZS)		12
Leflunomide (LEF)		11
• <b>Combination therapy</b>	531	49
As initial treatment		21
MTX + CQ		16
MTX + HCQ		9
MTX + LEF		5

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## *Follow up ( I )*

	<i>BL</i>	<i>6 m</i>	<i>12 m</i>	<i>18 m</i>
HAQ (mean)	1.5	0.9	0.7	0.7
DAS28 (mean)	6.5	4.5	4.2	4.2
<b>Remission</b>				
DAS28 0-2.59 (%)	0.2	15	17	18
ACR-ccr (%)	0.0	10	14	14

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**DAS28**: remission: 0-2.59 / low: 2.60-3.21 / moderate: 3.22-5.09 / high:  $\geq 5.10$

## *Follow up ( II )*

- **Change of diagnosis** 1.5 %  
Lupus (4), undif.polyarthritis (4),  
Spondyloarthropathies (2), others (5)
- **Lost of follow up** 4 %
- **Mortality** 0.5 %  
Sepsis (2), Asthma crisis (1),  
Renal insufficiency (1), Beçhet (multiorg.)

## PREDICTORS OF POOR PROGNOSIS

## GLADAR

- 
- Female ✓
  - Early age at onset ✓
  - Early morning stiffness (>60m) ✓
  - Symptom duration >6 week ✓
  - RF (+) ✓
  - DAS28 (high) ✓
  - HAQ (>1) ✓
  - HLADR4 ?
  - Disease duration without DMARDs ✓
  - S-E status / Education (low) ✓
  - Erosions ✓
  - Extra-articular manifestations ✓

# GLADAR COHORT

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## *Conclusions*

- First inception cohort of Latin American patients with early RA observed in their countries of origin and treated by their local rheumatologists
- Both the size and origin of this cohort make it unique
- High incidences of erosions, and high baseline disease activity and symptoms duration (DAS28), suggest a more aggressive disease in the Latin-American population at this early stage

# GLADAR – PARTICIPANTS

## ARGENTINA

Sacnun Monica  
Pons-Estel Bernardo  
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## COSTA RICA

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# GLADAR – PARTICIPANTS

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Camargo Eylen

Herrera Jose Antonio  
Paul Moya Hernando

Millan Alberto  
Rodriguez Martin



# ETHNIAS – OPERATIONAL DEFINITION

**Place of birth: patient, parents, grandparents**  
**Anthropomorphic characteristics**

## Individuals born in Latin America

- **Caucasians**  
4 European ancestors
- **Mestizos**  
Europeans & Amerindian ancestors
- **Afro-Latin-Americans**  
At least 1 African ancestor
- **Amerindians**  
4 Amerindian ancestors

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## **First Latin-American Consensus of RA Treatments (Quito, Sep/03)**

### ***CONCLUSIONS***

The consensus results and recommendations of this effort to delineate RA management in Latin America are contained in this manuscript, which has been reviewed by participant societies and authors during 2004/2005 and endorsed by PANLAR

# GLADAR COHORT

## Rheumatoid factor: sero (+) vs. sero (-)

### Variables

- Age at onset and diagnosis
- Extra-articular manifestations
- Infections
- Osteoarticular deformities
- Treatments
  - Use of DMARDs
  - Surgical interventions
- X-ray changes
- Number of admissions
- DAS28 - HAQ - ACR remission scores

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Use of DMARDs = sero (+) 93.4% vs. sero (-) 85.9%  $p < 0.001$