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MYELODYSPLASTIC SYNDROMES

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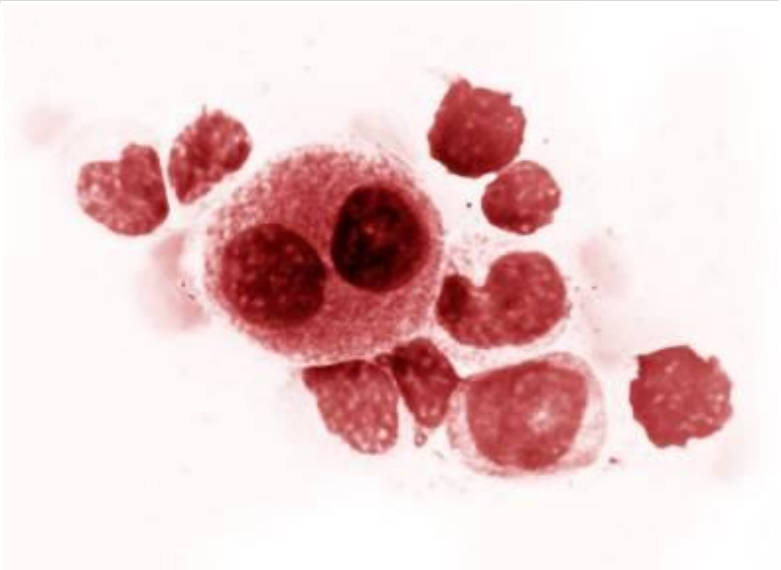

The European MDS studies coordination office

Supporting Clinical Research, Education and Consulting in the field of MDS across Europe

FISM Torino, 1. Apr. 2014

MDS Clinical Trials in Europe 2014

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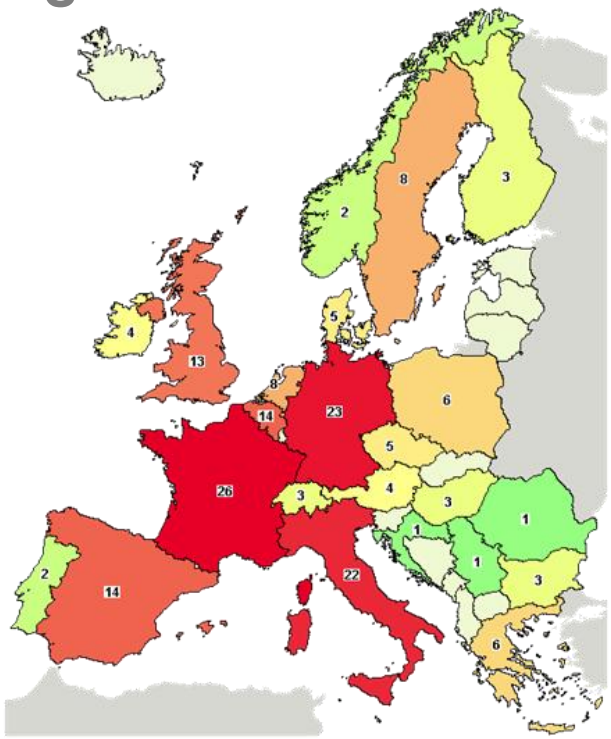
380 world wide clinical trials in MDS (open trials/known status)
72 European MDS clinical trials currently running

France	– 26 trials
Germany	– 23 trials
Italy	**– 22 trials**
Spain	– 14 trials
Great Britian	– 13 trials

The French Groupe Francophone des Myélodenysplasies (GFM) and the German MDS study group (GMDS-SG) sponsor 14 clinical trials in MDS

GMIHO (Dresden, Germany) is a specialist "Principal Investigator Network", which pools scientific expertise to offer an efficient infrastructure for clinical trials. Sponsors 3 clinical trials in MDS



Trends in MDS

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The Industry has MDS candidate drugs in development in Phase II and will need to launch Phase III trials in the next 5 years.

1. International trials are required to enroll enough patients
2. EC statistics 2007 – 2009 showed a 10% drop in clinical trials in the EU and a 33% drop in the number of EU patients entering clinical trials
3. MDS has become a widely studied disease where both, French GFM and German MDS study groups are very active.
4. MDS classification has become more complex and changes in clinical trial structure must reflect that there are smaller subgroups which require more sites

Over the next 5-7 years new medications in MDS will come into clinical testing, **international clinical trials** are necessary

*Market data from Global data 2012

EMSCO: MDS Studies Coordination Office

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Phase 1:

An Office has been set-up located in Dresden and administered by the GMIHO in Berlin

Phase 2 (2013):

1. Sustainable and financially independent EMSCO – external funding
2. Website, logo
3. Common trials (GFM/GMDS-SG) are in planning with the goal to identify hurdles and practical problems (e.g. submission to IRB and national authorities, insurance, central randomization, monitoring etc.)

www.emsco.eu

Supported by ELN

Phase 3 (2014/2015)

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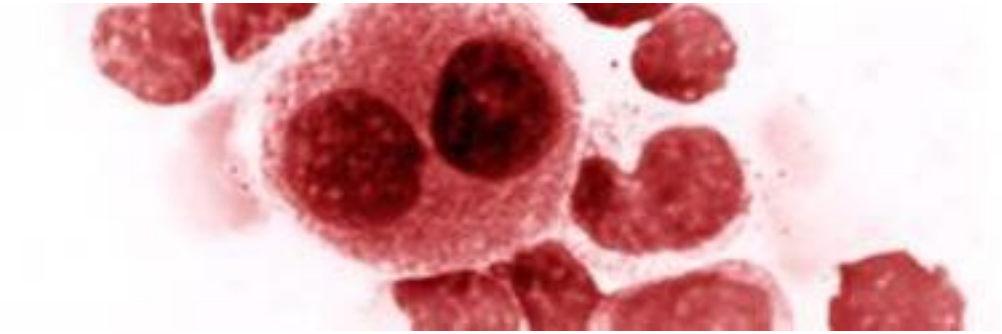
Three Pillars of EMSCO

Academic Clinical Research

Education

Consulting

- **European Platform** for MDS trials
- **Single-point of contact** - efficient and coordinated European trials in MDS
- **Standardization** of SOPs and treatment paradigms – reduces regulatory uncertainty regarding international trials
- **Improvement in best practices** and comparability of trial results across national borders



Phase 3 (2014/2015)

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Academic Clinical Research

SPONSOR	TITLE	PARTICIPANTS
Groupe Francophone des Myélodysplasies	A Randomized Phase III study of Decitabine with or without Hydroxyurea versus Hydroxy-urea in patients with advanced proliferative Chronic Myelomonocytic Leukemia	FRANCE GERMANY ITALY
GMIHO INNOVATION IN HEMATOLOGY AND MEDICAL ONCOLOGY	Prospective validation of a predictive model of response to romiplostim in patients with IPSS low or intermediate-1 risk myelodysplastic syndrome (MDS) and thrombocytopenia	GFM GMDSSG *FISM?*

International Trial Challenges

Some Critical Questions:

- Can the costs be supported in an IIT Setting?
- Who Should be the Sponsor?
- Costs Positions (i.e. IRB, MoH, Audits) differ between EU member states
- Reimbursement expectations between sites of EU member states
- Labels and Distribution of the Study Drug becomes complex (Annex 13) for shipping between EU member states

GFM DACHY CMML – TRIAL STARTUP TIMELINE

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CMML	Year	2014																																	
	Month	Feb				Mar				Apr				May				Jun					Jul				Aug				Sep				Oct				Nov			
STUDY SET-UP	Week	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W5	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4
TASK LIST	Responsible																																							
Feasibility	GMIHO									14 sites germany																																
Contracts with financier	GMIHO									GFM with GMIHO																																
delegation log	GMIHO																																								
protocol adaptation	GWT																																								
protocol review	EMSCO																																								
preparation of ISF	GWT																																								
Informed Consent	GWT																																								
Monitoring Manuel	GWT																																								
Patient Insurance	GFM																																								
Central Pharmacy/Label	GWT/TUD																																								
Reg. submission docs	GWT																																								
compile submission docs	GWT																																								
DSMB set-up / management	EMSCO																																								
eCRF / database system	GFM																																								
FRANCE submission	GFM																	60 days																							
EC FRANCE	GFM																		60 days																						
EC Italy	Italy																		60 days																						
EC Germany	GWT																		60 days	sitzung 20.MAY																				
German site contracts	EMSCO																																								
Set up site binders eTMF	GWT																																								
Assure Drug Supply	GFM/JnJ																																								
Central Lab setup	GWT																																								
Reg Doc Setup	GWT																																								
investigators meeting	GFM																																								
Monitor/CRA Training	GWT																																								
1st site Initiation Visit	GWT																										site initiation														
FPFV																													recruitment												

EUROPE – TRIAL STARTUP TIMELINE

EMSCO MYELODYSPLASTIC SYNDROMES

EUROPE	Year	person	hours	2013				2014				2014																							
	Month			Nov	Dec				Jan				Feb				Mar				Apr				May					Jun				Jul			
STUDY SET-UP	Week				W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W1	W2	W3	W4	W5	W1	W2	W3	W4	W1	W2	W3	W4
TASK LIST	**Responsible**																																		
kickoff-meeting internal	GMIHO																																		
EudraCT	GMIHO																																		
delegation log (FR)	GMIHO	SF	38																																
protocol draft	GMIHO	KL	60																																
protocol AMGEN - review	AMGEN	SF																																	
Informed Consent	GWT		12																																
Feasibility Germany	GMIHO	NA	40															20 sites germany																	
Qualification Germany	GMIHO	SF	40															20 sites germany																	
Feasibility France	GFM																	30 sites France																	
Contracts financier/lab	GMIHO	CH	60																																
protocol final	GMIHO	SF	33																																
Central Pharmacy/label	GWT /TUD																																		
final synopsis	U Platzbecker																																		
Updated IB / IMPD Romipl	GWT/AMGEN																																		
Patient Insurance	GMIHO		60																																
Reg. submission docs	GWT	CH	40																																
compile submission docs	GWT		10																																
signatures for submission	GMIHO																																		
eCRF / database system	GWT		100																																
Data Manuel	GWT																																		
GERMANY BOB	GWT	SF	60																					60 days											
EC FRANCE	GWT																							60 days											
EC Germany	GWT																					sitzung		sitzung 20.MAY -- 60 days											
Patient/Study specifc manuals	GWT																																		
Central Lab setup	GWT																																		
SAP	FL																																		
Pharmacovig Manuel	GWT																																		
Site Contact/Reg Doc Setup	GWT																																		
Site Contracts	GWT																																		
Set up site binders eTMF	GWT																																		
investigators meeting	GMIHO																																		
Monitoring Manual	GWT																																		
Monitor/CRA Training	GWT																																		
1st site Initiation Visit	GWT																															site initiation			
FPFV (3 week course)																																recruitment		

Ongoing EMSCO Activities

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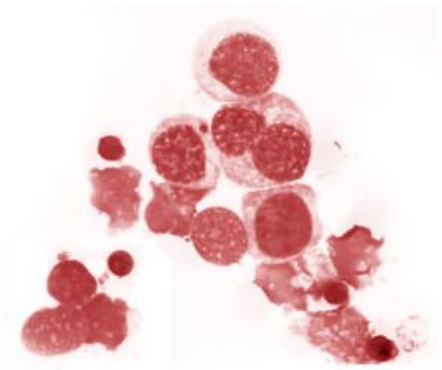
MYELODYSPLASTIC SYNDROMES

1. Inter-european clinical trials in MDS (EUROPE, CMML DAC-HY)
2. European site mapping – key/prime sites for MDS clinical trials
3. Organization of MDS Colloquium Mar. 2014
4. Organization of 3rd French-German MDS meeting Berlin, 10-11 Sep. 2014 – *Italy is Invited to participate!*
5. Creation of „open source“ clinical trial documents (i.e. contract templates, eCRF)
6. Establish competency center for MDS
7. Invite sites and Investigators to participate in EMSCO and become listed on the website



Promotions

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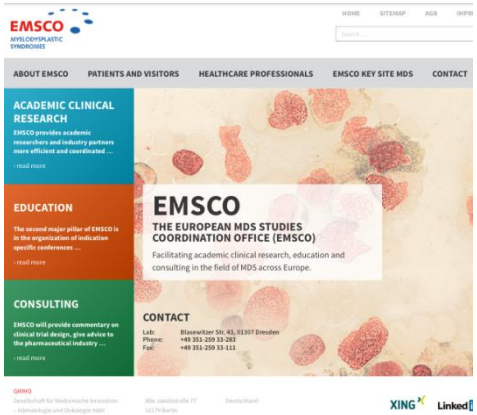
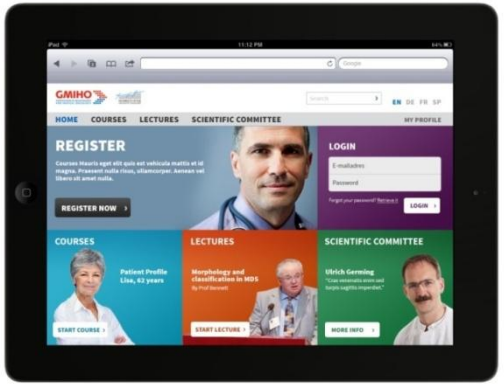


www.emsco.eu

Newsletter:
Reaching 2000 Hematologists in Germany



Websites:
Educational material in cooperation with Prof. U. Germing

www.mdsdiagnosis.com

We would like Italy to offer CME points for this site!

Mission Statement EMSCO

The European MDS studies coordination office (EMSCO)- Facilitating academic clinical research, education and consulting in the field of MDS across Europe

EMSCO builds bridges between academic and pharmaceutical clinical developers by:

- Facilitating research
- Improving data quality
- Accelerating translation and optimizing trial recruitment in MDS to ultimately improve patient outcomes

Thank you for your attention!

EMSCO
MYELODYSPLASTIC SYNDROMES

EMSCO - European MDS Studies Coordination Office
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About EMSCO

EMSCO is a branch of the GMIHO which was initially founded by the **German Society of Hematology and Oncology** to facilitate clinical trials in Germany because German universities have been historically reluctant to take over sponsorship for investigator initiated clinical trials.

Recently GMIHO was taken over by the GWT which is a S.a.r.l. The owner of the GWT is the TUDAG which stands for the **Technical University of Dresden AG**. The primary goal of TUDAG is to support scientists in managing and sponsoring research projects. TUDAG (and like wise GWT und GMIHO) serve as a platform for scientists to conduct research projects with more flexibility than can be offered in a legal structure beholden to government regulation.

Funds gained through the projects however serve the public at the end, [as dictated by the charter of the TUDAG]. About 500 scientists use the above mentioned structure in Germany. Several trials of the German MDS SG have been carried out with GMIHO as Sponsor, e.g. LEMON5 trial and the German MDS Register.

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