The 1200 Patients Project

Mark J. Ratain, M.D.

University of Chicago

Genomic Medicine Centers Meeting II

Bethesda, MD

December 5, 2011

The 1200 Patients Project

The Future of Personalized Medicine

Center for Personalized Therapeutics

THE UNIVERSITY OF CHICAGO

http://cpt.uchicago.edu/

People

- Home
- 1200 Patients Project
- Get Involved
- People
- Contact Us
- What's New
- What is Pharmacogenomics?
- Fellowship Opportunities

SEARCH

CENTER FOR PERSONALIZED THERAPEUTICS
THE UNIVERSITY OF CHICAGO

The 1200 Patients Project

OTHER RESOURCES

- UChicago Medical Center
- Comprehensive Cancer Center
- University of Chicago Biological Sciences Department

Mark Ratain, M.D.

Director

Phone: (773) 702-4400
Fax: (773) 702-3163
mratain@medicine.bsd.uchicago.edu

Peter H. O'Donnell, M.D.

Assistant Director, Principal Investigator-The 1200 Patients Project

Phone: (773) 702-7564
Fax: (773) 702-3163
podonnel@medicine.bsd.uchicago.edu

Nancy J. Cox, Ph.D.

Associate Director, Genomics and Informatics

Phone: (773) 834-1001
Fax: (773) 702-2567
ncox@bsd.uchicago.edu

M. Eileen Dolan, Ph.D.

Associate Director, Education and Training

Phone: (773) 702-4441
Fax: (773) 834-0188
edolan@medicine.bsd.uchicago.edu

Michael Maitland, M.D., Ph.D.

Assistant Director, Physician Education

Phone: (773) 834-8981
Fax: (773) 834-0188
mmaitlan@medicine.bsd.uchicago.edu

Barriers to implementation of pharmacogenomic diagnostics

- Lack of MD knowledge
- Availability of tests
- Costs and reimbursement
- Delay in obtaining results
- MD concerns regarding interpretation

Implementation of PG diagnostics

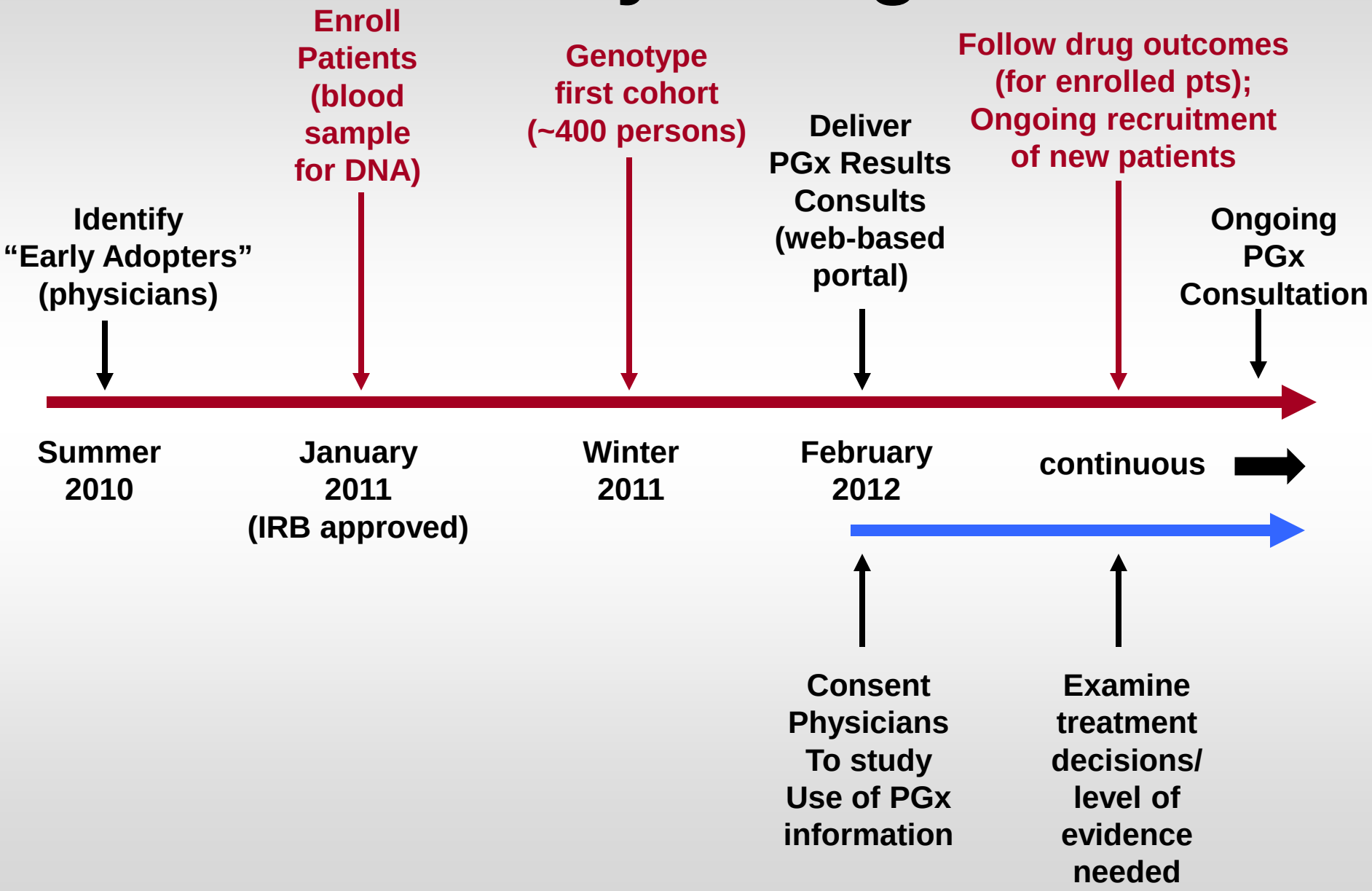
Barriers

- Lack of MD knowledge
- Availability of tests
- Costs and reimbursement
- Delay in obtaining results
- MD concerns regarding interpretation

Solutions

- Creation of a web portal
- All relevant PG variants
- No marginal cost
- Preemptive genotyping
- Results interpreted as individualized virtual pharmacogenomic consult

Study Design



Early-Adopter Physicians

Cardiology

Oncology

Rheumatology

Primary Care

Executive Health

Cardiology

Oncology

Primary Care

Oncology

Primary Care

Gastroenterology

Hepatology

Pulmonology

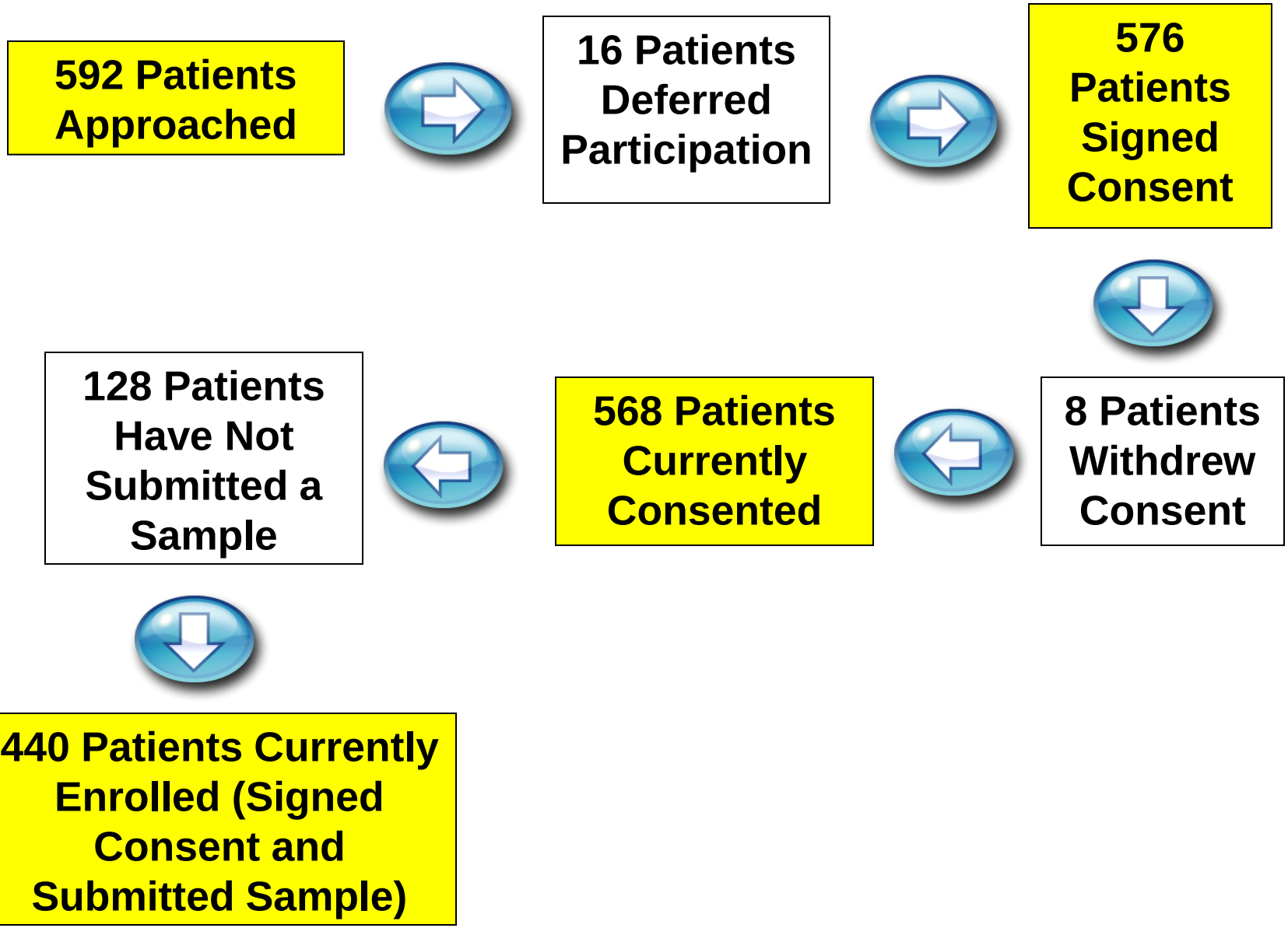
Patient Eligibility

- Adults receiving ongoing, outpatient care from one of the study co-investigator physicians at The University of Chicago
- Must be taking at least 1 regularly-used prescription medication, but not more than 6
  - Or >65 yrs or expected to require 1 within 5 yrs
- Patients excluded if acute or chronic disease would preclude them from being followed for at least 3 years
- Patients excluded who have undergone, or are being actively considered for, liver or kidney transplantation

1200 Patients Project Update

- IRB Approved: January 14, 2011
- First Consented Patient: January 20, 2011
- First Enrolled Patient (sample collected): January 25, 2011

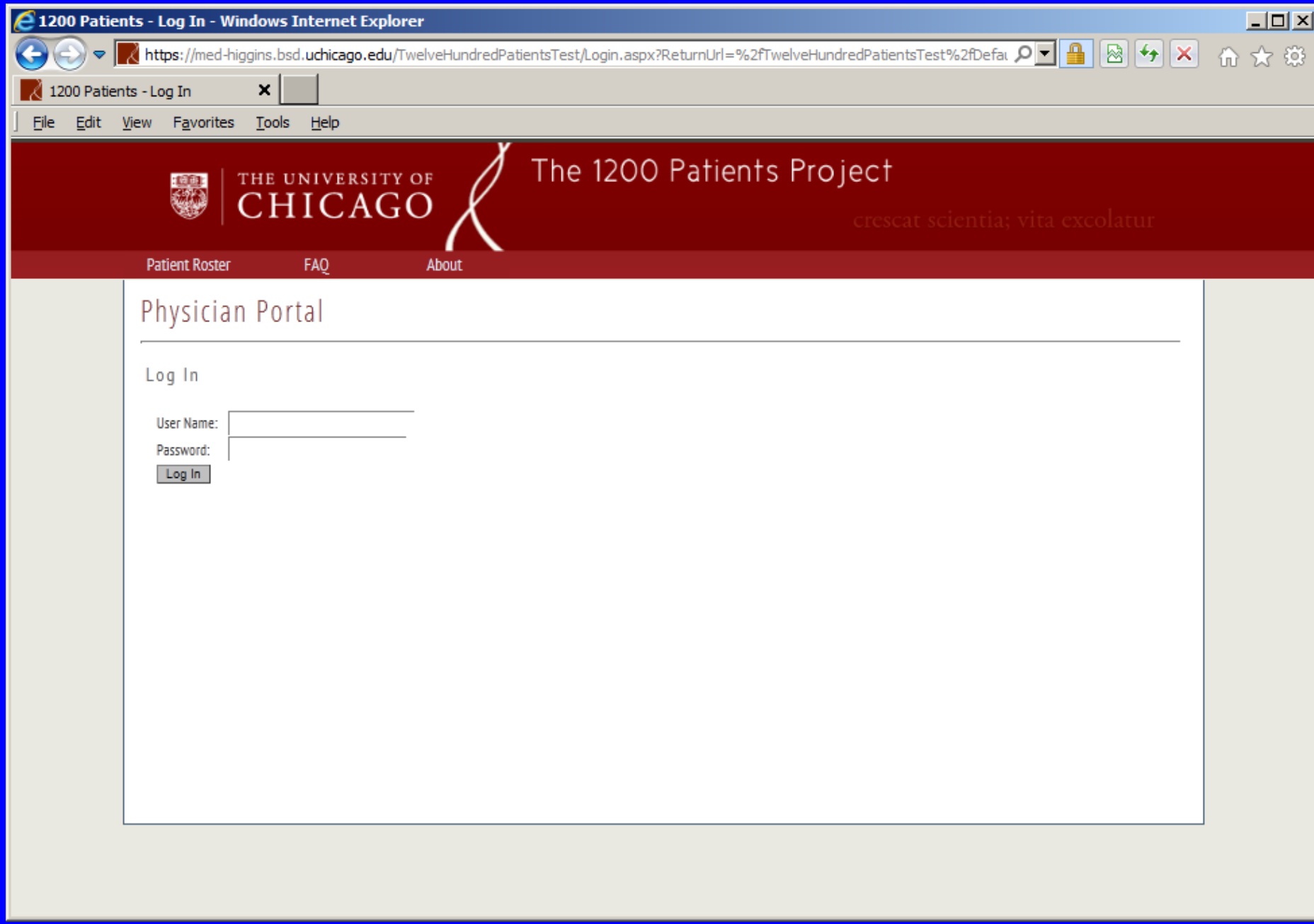
Enrollment Update



Most Frequently Prescribed Medications for Enrolled Patients

Drug	Number of Patients	Percentage
hydrochlorothiazide	59	16%
atorvastatin	55	14%
amlodipine	41	11%
lisinopril	40	11%
levothyroxine	38	10%
metoprolol	33	9%
simvastatin	31	8%
prednisone	27	7%
atenolol	24	6%
omeprazole	23	6%
warfarin	22	6%
azathioprine	22	6%
furosemide	20	5%
naproxen	19	5%

(all other medications taken by <5% of patients)


1200 Patients - Log In - Windows Internet Explorer
https://med-higgins.bsd.uchicago.edu/TwelveHundredPatientsTest/Login.aspx?ReturnUrl=%2fTwelveHundredPatientsTest%2fDefau
1200 Patients - Log In
File Edit View Favorites Tools Help
THE UNIVERSITY OF CHICAGO
The 1200 Patients Project
crescat scientia; vita excolatur
Patient Roster FAQ About
Physician Portal
Log In
User Name:
Password:
Log In

1200 Patients - Patient Info - Windows Internet Explorer

https://med-higgins.bsd.uchicago.edu/TwelveHundredPatientsTest/PatientInfo.aspx

1200 Patients - Patient Info

File Edit View Favorites Tools Help

THE UNIVERSITY OF CHICAGO

The 1200 Patients Project

crescat scientia; vita excolatur

Patient Roster FAQ About Logout

Physician Portal

Patient Name : Clark, Rebecca
Sex : F
DOB : 11/15/1956

Back to Patient Roster

Legend - Levels of Evidence

Level 1 - From a well-performed study including at least 1000 patients and replicated in another independent population of at least 1000 patients.
Level 2 - Evidence from a single well-performed study of at least 100 patients implicates the relationship.
Level 3 - Evidence from a relatively small single study (<100 patients) or from several smaller studies implicate the relationship; similarly-executed contradictory studies may exist.

Legend - StopLight Definitions

Favorable: your patient has a genotype which suggests an improved chance of benefit or a decreased risk of toxicity with this medication.
Caution: your patient has a genotype associated with possible undesirable outcomes when using this medication.
Warning: your patient has a genotype which confers a significant increase in risk with use of this medication.
There is no known pharmacogenomic information relevant to this medication.

Patient Home | Search Drugs/Diseases for Relationships

Patient's Current Medications

Medication	Patient->Drug Association	Level of Evidence	Evidence References
amlodipine		Level 2	PMID: 19907160
omeprazole		Level 2	PMID: 16413245 PMID: 18294333

https://med-higgins.bsd.uchicago.edu/TwelveHundredPatientsTest/PatientI...

1200 Patients - Patient Info - Windows Internet Explorer

https://med-www02.bsd.uchicago.edu/TwelveHundredPatients/PatientInfo.aspx

1200 Patients - Patient Info

File Edit View Favorites Tools Help

THE UNIVERSITY OF CHICAGO

The 1200 Patients Project

crescat scientia; vita excolatur

Patient Roster FAQ About Logout

Physician Portal

Patient Name : Smith, Mike
Sex : M
DOB : 10/2/1948

Back to Patient Roster

Patient Home/Current Medications | Clinical Drug Summary | Search Drugs/Diseases

[Back to Meds]

Patient Specific Information for : adalimumab

Summary

Your patient has a genotype at the TNF gene promoter that predicts the highest likelihood of response to adalimumab based on changes in Disease Activity Score in 28 joints (DAS28) at 24 weeks.

In one study of 86 patients, the average improvement in the DAS28 was 0.83 in A/A patients, 1.50 in A/G patients and 2.64 in G/G patients (P < 0.0001). "Good responders" (as compared to moderate or non-responders) were always G/G.

In another study of 81 patients which demonstrated the same relationship, patients with the G/G genotype responded 88.2% of the time versus 68.4% of patients with the G/A genotype (P= 0.05). DAS28 Score improvements were higher in the G/G group (P= 0.04).

Evidence

Level 3 : Evidence from a relatively small single study (<100 patients) or from several smaller studies; similarly-executed contradictory studies may exist.

Primary Literature Sources

PMID: 16720636
PMID: 17343250

Legend - StopLight Definitions

- Favorable: your patient has a genotype which suggests an improved chance of benefit or a decreased risk of toxicity with this medication.
- Caution: your patient has a genotype associated with possible undesirable outcomes when using this medication.
- Warning: your patient has a genotype which confers a significant increase in risk with use of this medication.
- There is no known pharmacogenomic information relevant to this medication.

Legend - Levels of Evidence

Level 1 - From a well-performed study including at least 1000 patients and replicated in another independent population of at least 1000 patients.
Level 2 - Evidence from at least one well-performed study of at least 100 patients.
Level 3 - Evidence from a relatively small single study (<100 patients) or from several smaller studies; similarly-executed contradictory studies may exist.

Legend - New Information Available

! - This symbol denotes that new patient specific information is available for this medication since physician's last login.

[Back to Meds]

Drug Specific Information for : adalimumab

Summary

Your patient has a genotype at the TNF gene promoter that predicts the highest likelihood of response to adalimumab based on changes in Disease Activity Score in 28 joints (DAS28) at 24 weeks.

In one study of 86 patients, the average improvement in the DAS28 was 0.83 in A/A patients, 1.50 in A/G patients and 2.64 in G/G patients ($P < 0.0001$). "Good responders" (as compared to moderate or non-responders) were always G/G.

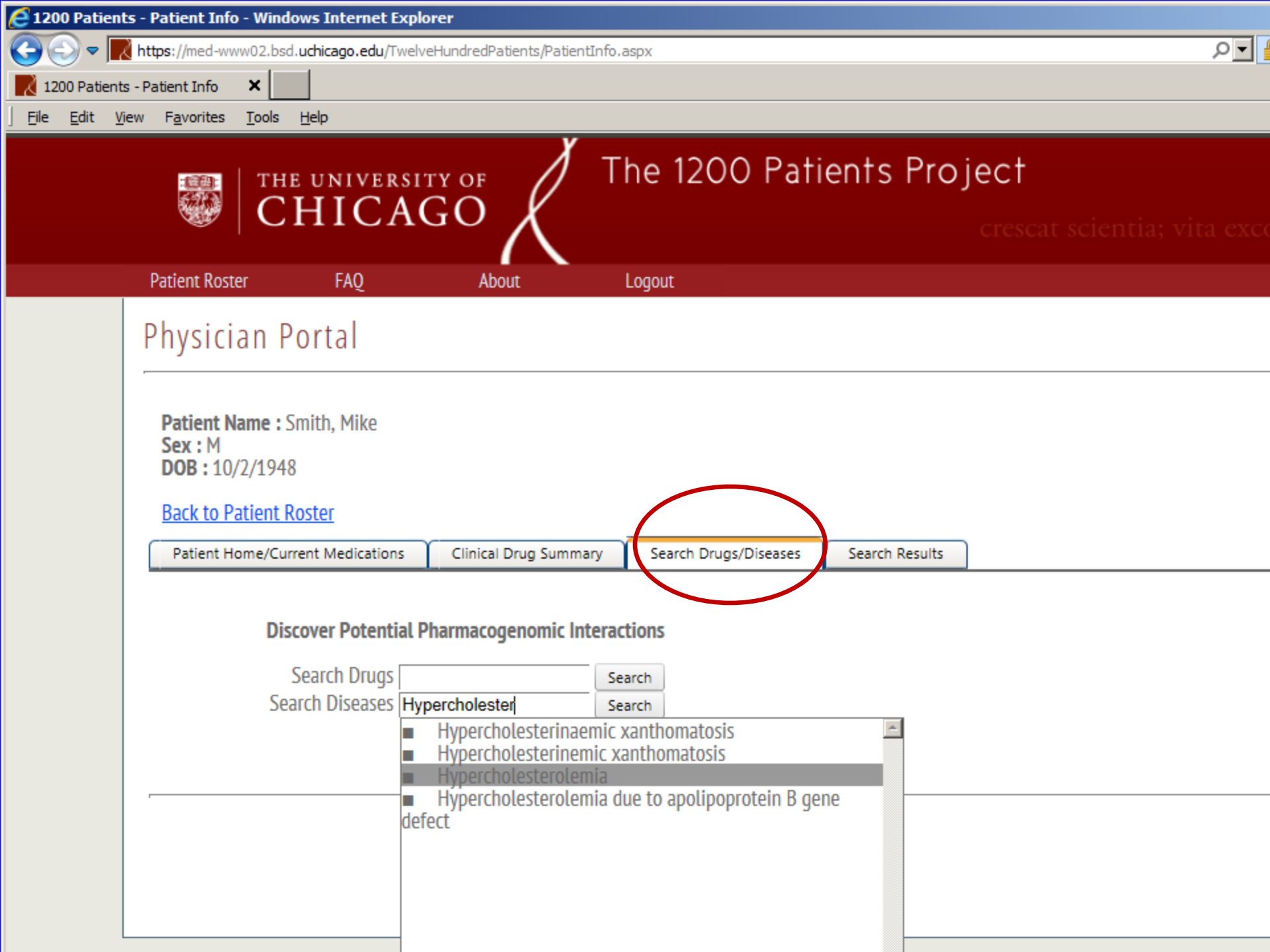
In another study of 81 patients which demonstrated the same relationship, patients with the G/G genotype responded 88.2% of the time versus 68.4% of patients with the G/A genotype ($P= 0.05$). DAS28 Score improvements were higher in the G/G group ($P= 0.04$).

Evidence

Level 3 : Evidence from a relatively small single study (<100 patients) or from several smaller studies implicate the relationship; similarly-executed contradictory studies may exist.

Evidence References

PMID: 16720636
PMID: 17343250


1200 Patients - Patient Info - Windows Internet Explorer
https://med-www02.bsd.uchicago.edu/TwelveHundredPatients/PatientInfo.aspx
1200 Patients - Patient Info
File Edit View Favorites Tools Help
THE UNIVERSITY OF CHICAGO
The 1200 Patients Project
Patient Roster FAQ About Logout
Physician Portal
Patient Name : Smith, Mike
Sex : M
DOB : 10/2/1948
Back to Patient Roster
Patient Home/Current Medications
Clinical Drug Summary
Search Drugs/Diseases
Search Results
Discover Potential Pharmacogenomic Interactions
Search Drugs
Search
Search Diseases
Hypercholester
Search
Hypercholesterinaemic xanthomatosis
Hypercholesterinemic xanthomatosis
Hypercholesterolemia
Hypercholesterolemia due to apolipoprotein B gene defect

Physician Portal

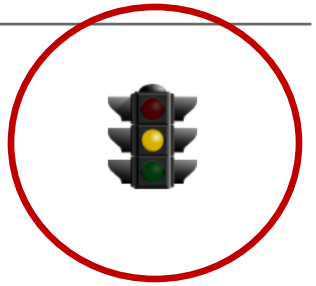
Patient Name : Smith, Mike
Sex : M
DOB : 10/2/1948

Back to Patient Roster

Patient Home | Current Medications | Clinical Drug Summary | Search Drugs/Diseases | Search Results

[Back to Drug List]

simvastatin is a possible drug for : Hypercholesterolemia



Summary

Your patient carries a genotype that confers a 17-fold odds ratio of risk for developing simvastatin-induced myopathy compared to individuals with no risk alleles.

This translates to an 18% cumulative risk of myopathy over 6 years, compared to 0.6% risk in those without the alleles. Almost all patients with the high-risk genotype who develop myopathy developed it within the first 8 months of therapy.

These data were first derived from a study of 175 individuals--and the results were replicated in a group of over 16,000 individuals--taking simvastatin at doses between 40-80 mg.

Another study of 509 patients taking statins found that those with your patient's genotype had a 50% incidence of either premature discontinuation of the drug, myalgias, or creatine kinase elevations >3 times the upper limit of normal, compared to a 27% incidence in patients with only one copy of the risk allele, and 19% in patients with no risk alleles (Ptrend = 0.01). In sub-group analysis, the adverse risks remained statistically significant and were greatest in the 162 patients taking simvastatin at 80 mg.

Published data do suggest the myopathy risk for simvastatin may be particularly due to use of the 80 mg dose, and recommendations against using this dose have been published.

Evidence
Level 2 : Evidence from at least one well-performed study of at least 100 patients.

Primary Literature Sources
PMID: 18650507
PMID: 19833260
PMID: 21675881

Legend - StopLight Definitions

- Favorable: your patient has a genotype which suggests an improved chance of benefit or a decreased risk of toxicity with this medication.
- Caution: your patient has a genotype associated with possible undesirable outcomes when using this medication.
- Warning: your patient has a genotype which confers a significant increase in risk with use of this medication.
- There is no known pharmacogenomic information relevant to this medication.

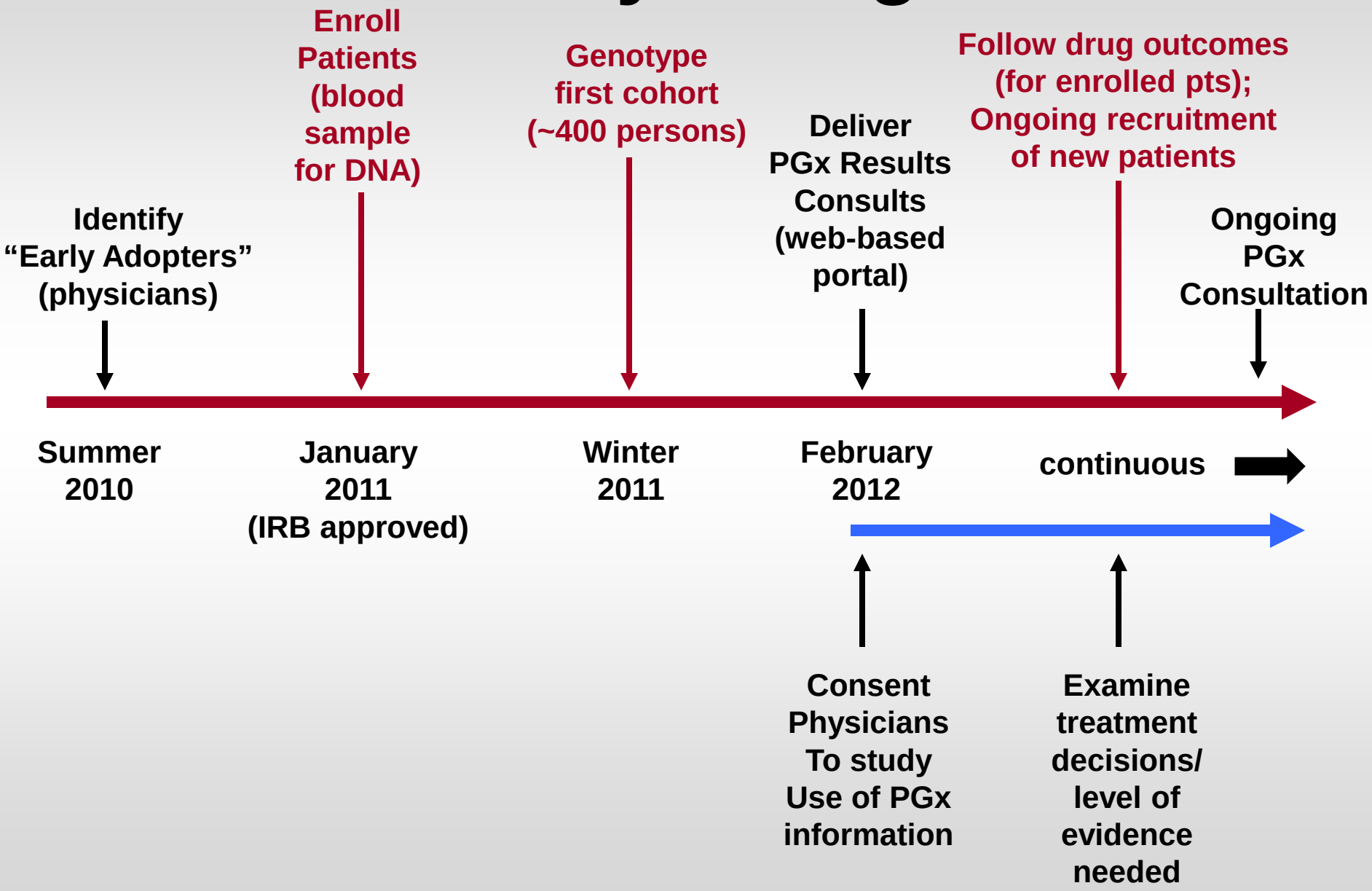
Legend - Levels of Evidence

Level 1 - From a well-performed study including at least 1000 patients and replicated in another independent population of at least 1000 patients.
Level 2 - Evidence from at least one well-performed study of at least 100 patients.
Level 3 - Evidence from a relatively small single study (<100 patients) or from several smaller studies; similarly-executed contradictory studies may exist.

Legend - New Information Available

- This symbol denotes that new patient specific information is available for this medication since physician's last login.

Study Design



Opportunity for collaboration

- **“Phase 2” randomized study of preemptive genotyping**
  - **Genotype all enrolled patients**
  - **Provide data to physicians for only half of the patients**
  - **Measure clinical outcomes**
    - **Genotype-associated adverse events**