East® Architect

Software for Designing, Simulating and Monitoring Clinical Trials

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Hrishikesh Kulkarni, Cytel Inc.

Sheetal Solanki, Cytel Inc.

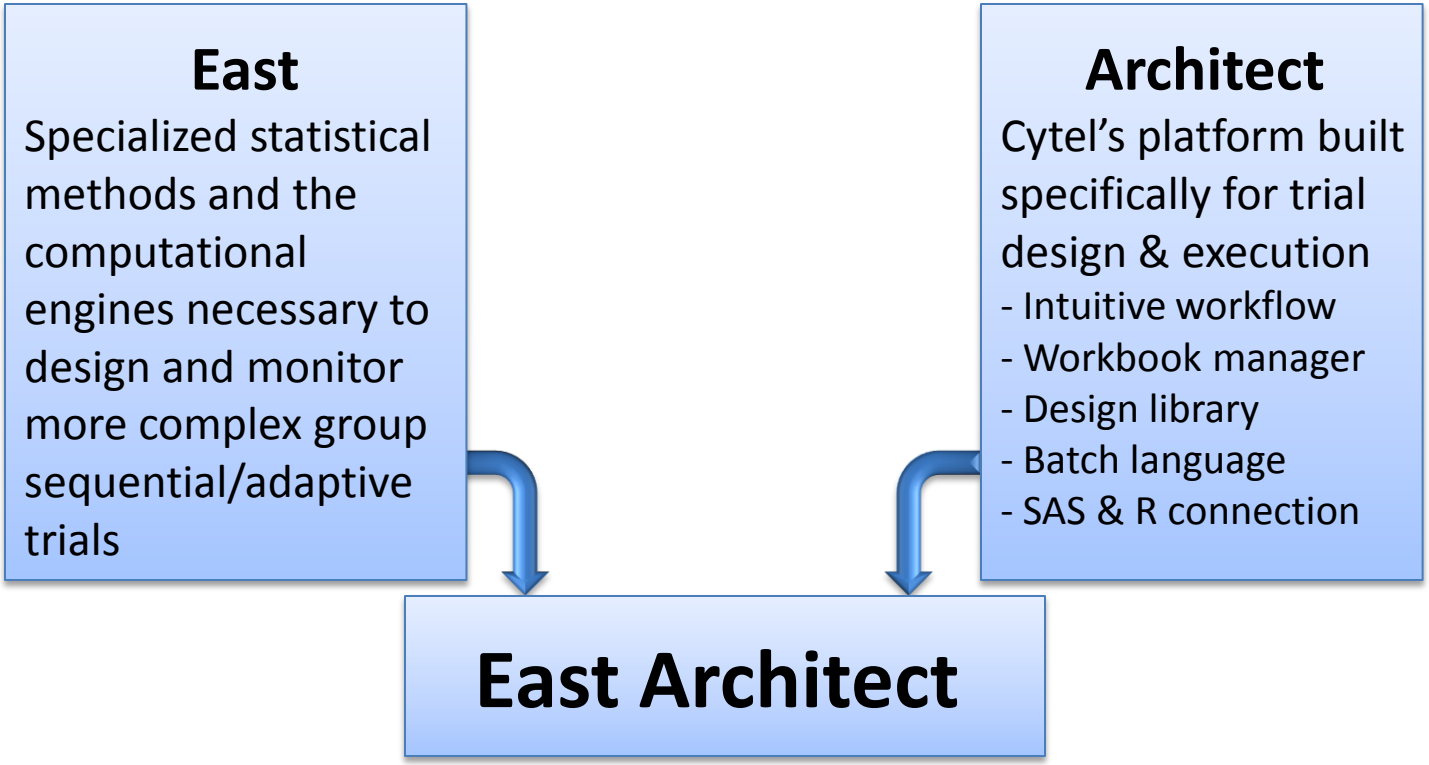
www.cytel.com

Agenda

- What is East® Architect?
- A tour through East Architect with a case study. Features covered on the way:
  - Design
  - Simulation
  - Interim Monitoring
- Canvas: A convenient reporting tool
- Other interesting features

What is East® Architect?

East: most widely used, validated software of it's kind, installed at every major pharma company, scores of specialty biotech and device developers, and the FDA



Case Study : Schizophrenia Trial

- Primary Endpoint: Change in Negative Symptoms Assessment (NSA) after 26 weeks
- At least a 2-point improvement is considered as significant
- Desired Power is 90% and level of significance is fixed to 2.5 %
- Common Standard Deviation is anticipated to be 7.5 units

Designing using East Architect

- Exhaustive creation and comparison of multiple designs
- Selection of designs based on some criteria using Filter
- Ability to establish stopping rules for efficacy and/or futility
- Ability to construct custom combinations of Efficacy and Futility stopping boundaries

Accrual/Dropout Effect in Simulations

	Wbk1:Des9	Wbk1:Des9:Sim1	Wbk1:Des9:Sim2	Wbk1:Des9:Sim3
Mnemonics	MN-2S-DI	MN-2S-DI	MN-2S-DI	MN-2S-DI
Test Parameters				
Trial Type	Superiority	Superiority	Superiority	Superiority
No. of Looks	3	3	3	3
Test Type	1-Sided	1-Sided	1-Sided	1-Sided
Specified α	0.025			
Specified Power	0.9			
Attained Power	0.9	0.901	0.869	0.827
Accrual & Dropout Parameters				
Accrual Rate	8			
Response Lag	26	26	26	26
Probability of Dropout	0	0	0.1	0.2
No. of Accrual Periods		1	1	1
Sample Size				
Maximum	723	723	723	723
Expected Under H0	558.166			
Expected Under H1	678.876			
Completers				
Maximum	723	723	650	578

Final Design for Monitoring

Design: Continuous Endpoint: Two-Sample Test - Parallel Design - Difference of Means

Test Parameters:

Design ID:	Des9
Trial Type:	Superiority
No. of Looks:	3
Test Type:	1-Sided
Specified α:	0.025
Attained α:	0.02
Specified Power:	0.9
Attained Power:	0.9

Model Parameters:

Test Statistic:	Normal
Input Method:	Individual Means
Mean Control (μ_c):	0
Mean Treatment (μ_{t1}):	2
$\delta = \mu_t - \mu_c$	
Under H0:	0
Under H1:	2
Std. Deviation (σ):	7.5
Allocation Ratio (n_t/n_c):	1

Boundary Parameters:

Spacing of Looks:	Equal
Efficacy Boundary:	LD (OF)
Futility Boundary:	LD (PK) (NB)

Accrual/Dropout Parameters:

Accrual Rate:	8
Response Lag:	26
Probability of Dropout:	0

Stopping Boundaries: Look by Look

Look #	Info. Fraction (s/s_max)	Sample Size (n)	Cumulative α Spent	Cumulative β Spent	Boundaries	
					Efficacy Z	Futility Z
1	0.333	449	0.0001	0.0452	3.7103	0.3764
2	0.667	690	0.006	0.0762	2.5114	1.2783
3	1	723	0.025	0.0998	1.993	1.993

Completers, Sample Size, Pipeline and Analysis Times: Look by Look

Look #	Info. Fraction (s/s_max)	Sample Size (n)	Completers (s)	Pipeline (n-s)	Time of Look	Incr. Boundary Crossing Prob.			
						Under H0		Under H1	
						Efficacy	Futility	Efficacy	Futility
1	0.333	449	241	208	56.125	0.0001	0.6467	0.0505	0.0452
2	0.667	690	482	208	86.25	0.0059	0.2657	0.6077	0.031
3	1	723	723	0	116.375	0.0139	0.0678	0.2421	0.0236

Sample Size Information:

	Maximum	Expected H1	Expected H0
Sample Size (n)	723	678.876	558.166
Sample Size Treatment (n_t)	361	337.68	268.047
Sample Size Control (n_c)	362	338.041	268.776
Completers (s)	723	522.991	345.817
Completers Treatment (s_t)	361	261.315	172.544
Completers Control (s_c)	362	261.676	173.273
Accrual Duration	90.375	68.255	62.711
Study Duration	116.375	94.255	88.711
Information	3.213	2.324	1.537

Decision Making using Interim Monitoring

- Analyzing data at regular time intervals
- Boundaries, Repeated CI computed at each look
- Final Inference computed at the end
- Other useful functionalities
  - Custom charts, tables and graphs
  - Conditional Power Calculator
  - R integration

Canvas

- Feature to create customized reports
- Can extract data from any output window of East and drag-n-drop to Canvas
- Consolidated report can be presented in the PDF or HTML format

Other Interesting Features

Design

- Selection of rules for establishing efficacy/futility boundaries at selected interim looks
- Boundary family combinations to determine efficacy and futility boundaries

Simulations

- Stratified simulations
- Adaptive simulations

IM & Analysis

- R and SAS integration
- Conditional Power calculations for adaptive trials
- Conditional simulations

Thank you!

Q & A

hrishikesh.kulkarni@cytel.com
sheetal.solanki@cytel.com

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