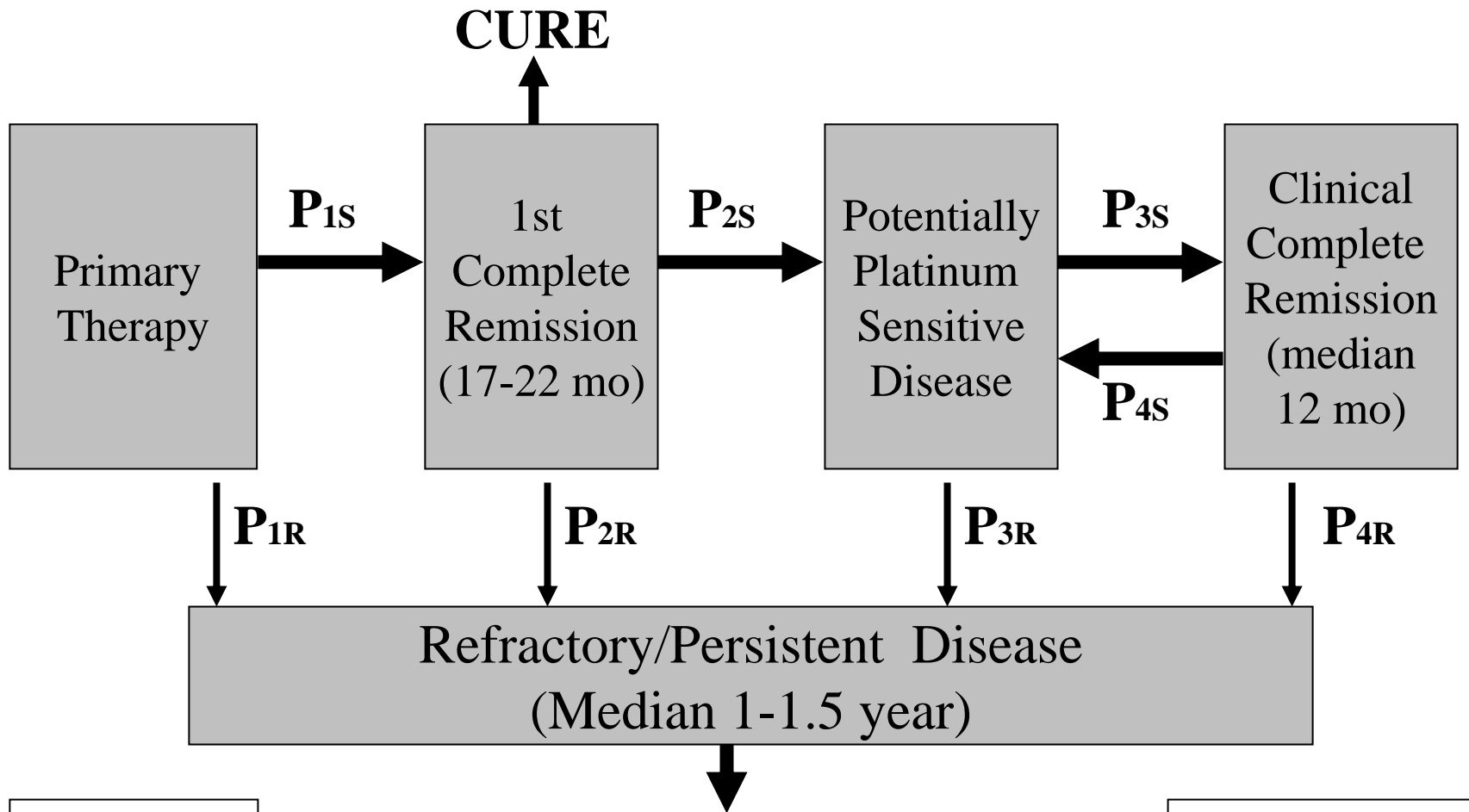


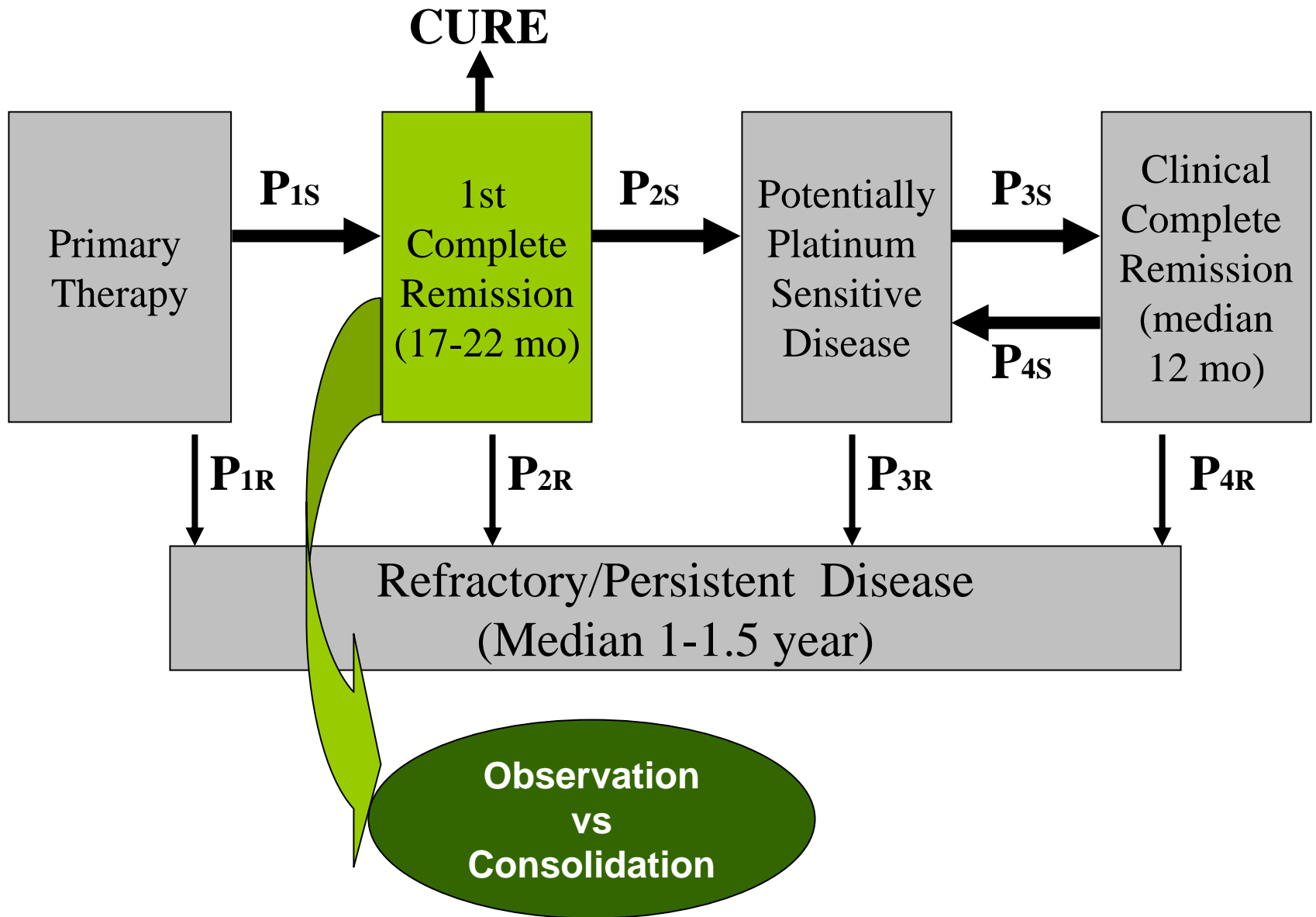
Endpoints in Ovarian Cancer Clinical Trials

Recurrent Disease



(From
GOG 111)
 $P_{1S} = 51\%$
 $P_{1R} = 49\%$

Risk Estimates
 $P_{3S} = 42\%$
 $P_{3R} = 58\%$
 $P_{4S} = 54\%$
 $P_{4R} = 46\%$



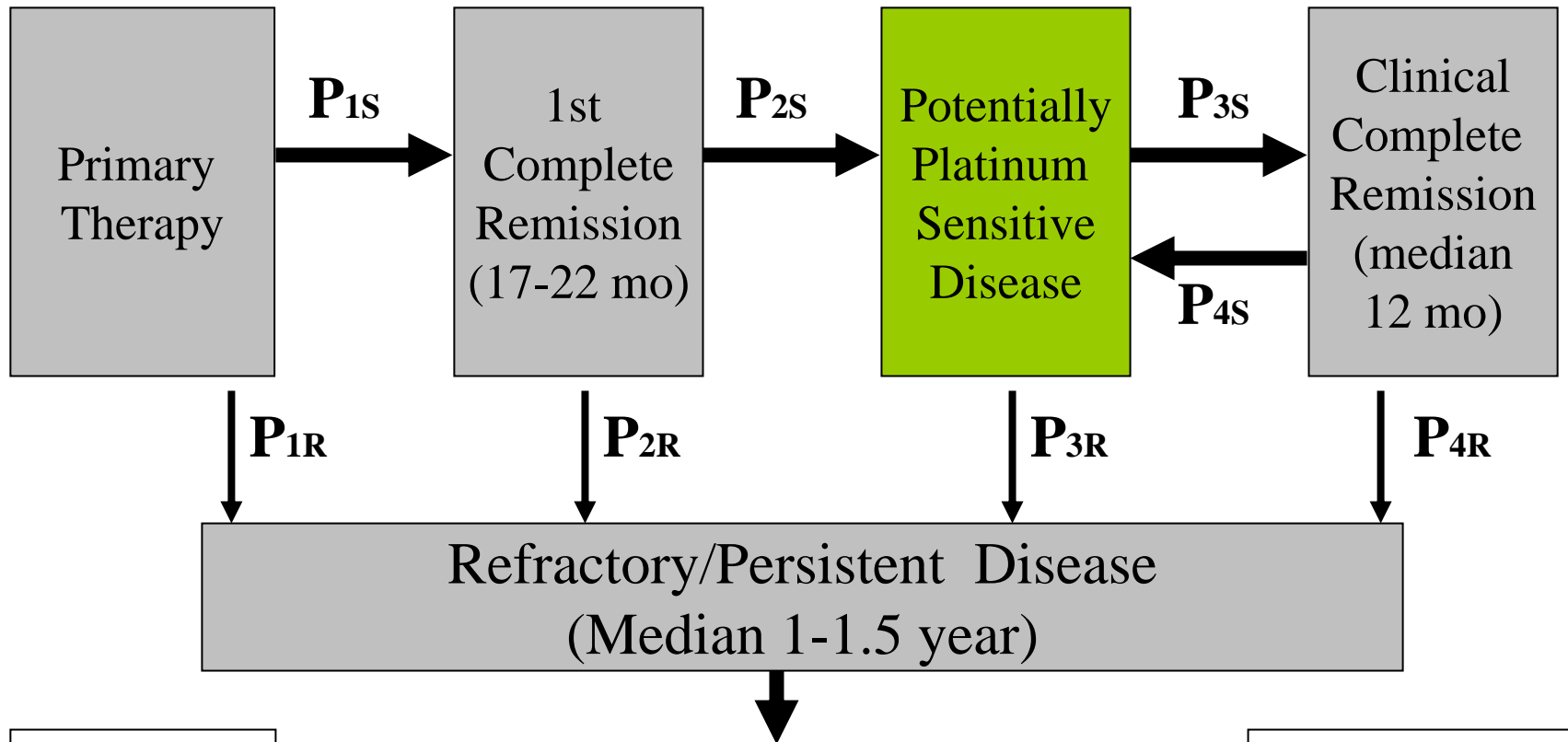
Negative Consolidation Trials

- Negative Survival Trials
 - Interferon alpha
 - High dose chemotherapy
 - WART
 - Extended Platinum Rx
 - Topotecan
 - Epirubicin
 - P32
 - Orgovanomab (Ovarex)
 - Yt90-muHMG1 (SMART)

Other trials

- Untested ideas
 - IP therapy
 - Vaccination
 - Anti-idiotypic CA125
 - Defined epitopes
 - Cell Derived Vaccines
 - Common biologics
 - EGFr antagonists
 - TKI's
- GOG 178
 - Positive PFS only
- Current Trials
 - Bevacizumab
 - Paclitaxel (Pcl) vs Polyglutamylated Pcl
- “After six” group

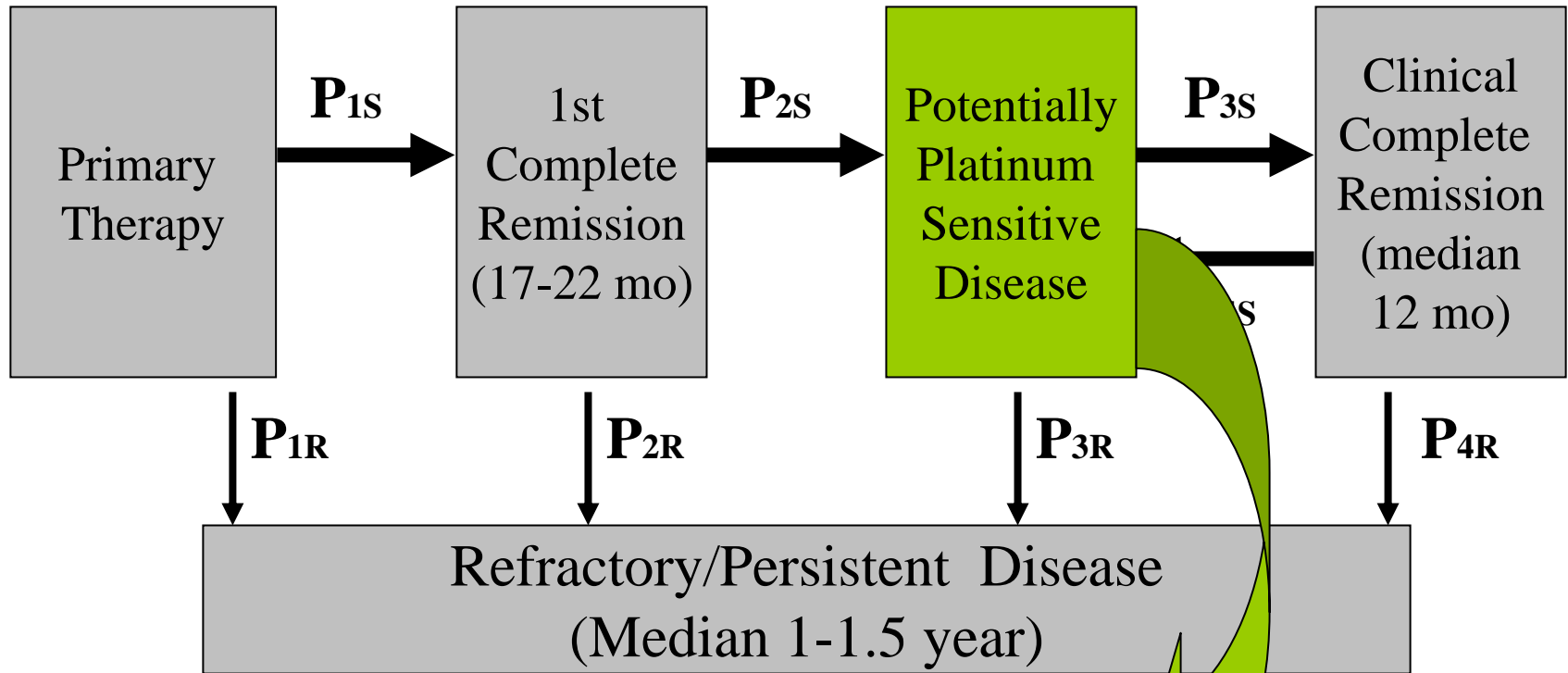
Endpoints for Platinum Sensitive Disease



(From
GOG 111)
 $P_{1S} = 51\%$
 $P_{1R} = 49\%$

Risk Estimates
 $P_{3S} = 42\%$
 $P_{3R} = 58\%$
 $P_{4S} = 54\%$
 $P_{4R} = 46\%$

Definition of Platinum Sensitive Disease



Platinum Sensitive: Recurrence more than 6 months after the last dose of platinum therapy

6-12 mo

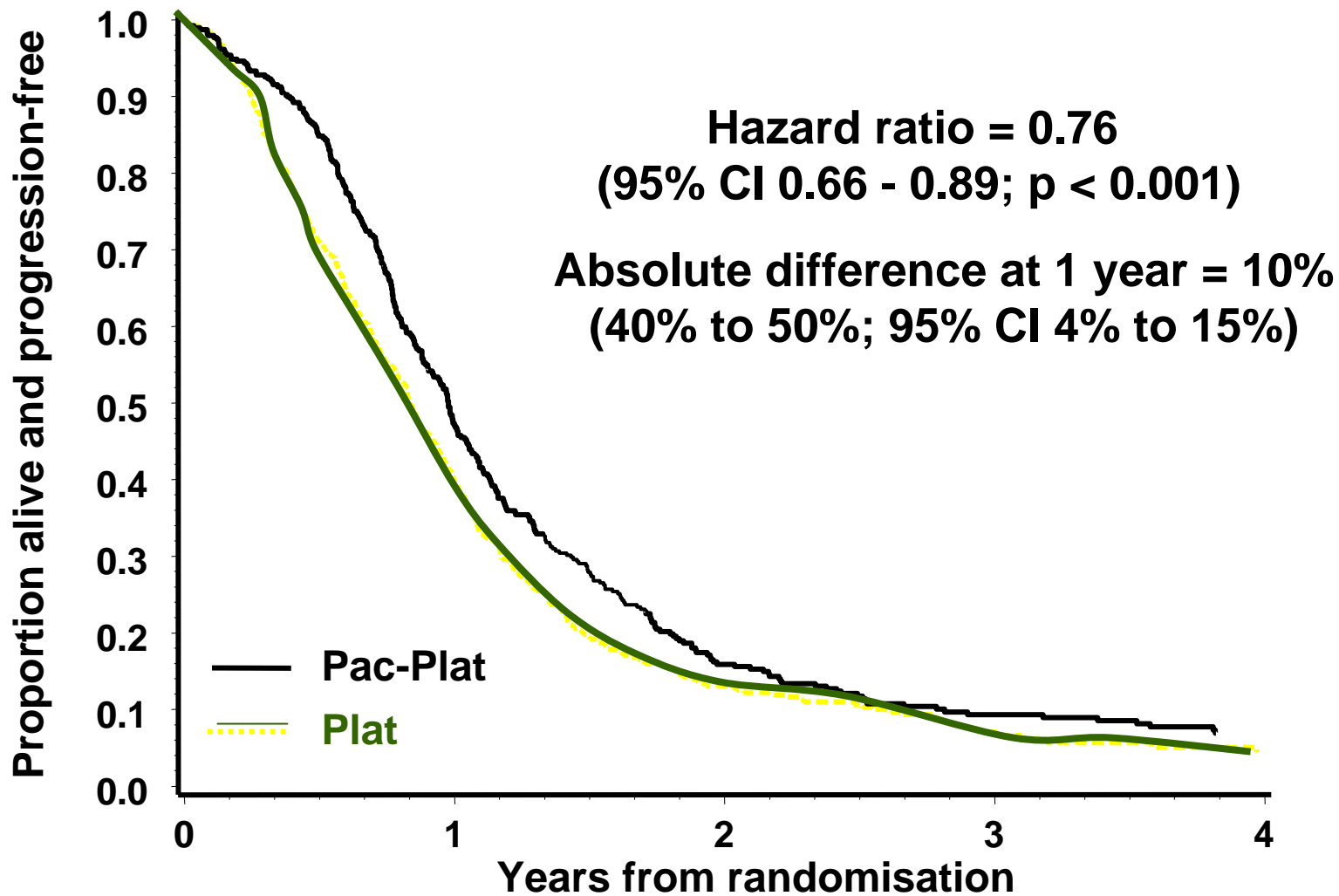
12-24 mo

>24 mo

TRIALS FOR PLATINUM SENSITIVE DISEASE

Trial	PFS	OS	CA125 POD?
ICON4 Plt + Tx	1 yr 50%*	2 yr 57%*	No
ICON4 No Tx	1 yr 40%	2 yr 50%	No
AGO Carb	5.8 mo	NR	No
AGO Carb + Gem	8.6 mo*	NR	No
Peg Lipo Dox	0.55** yr	2.07** yr	No
Topotecan	0.45 yr	1.34 yr	No

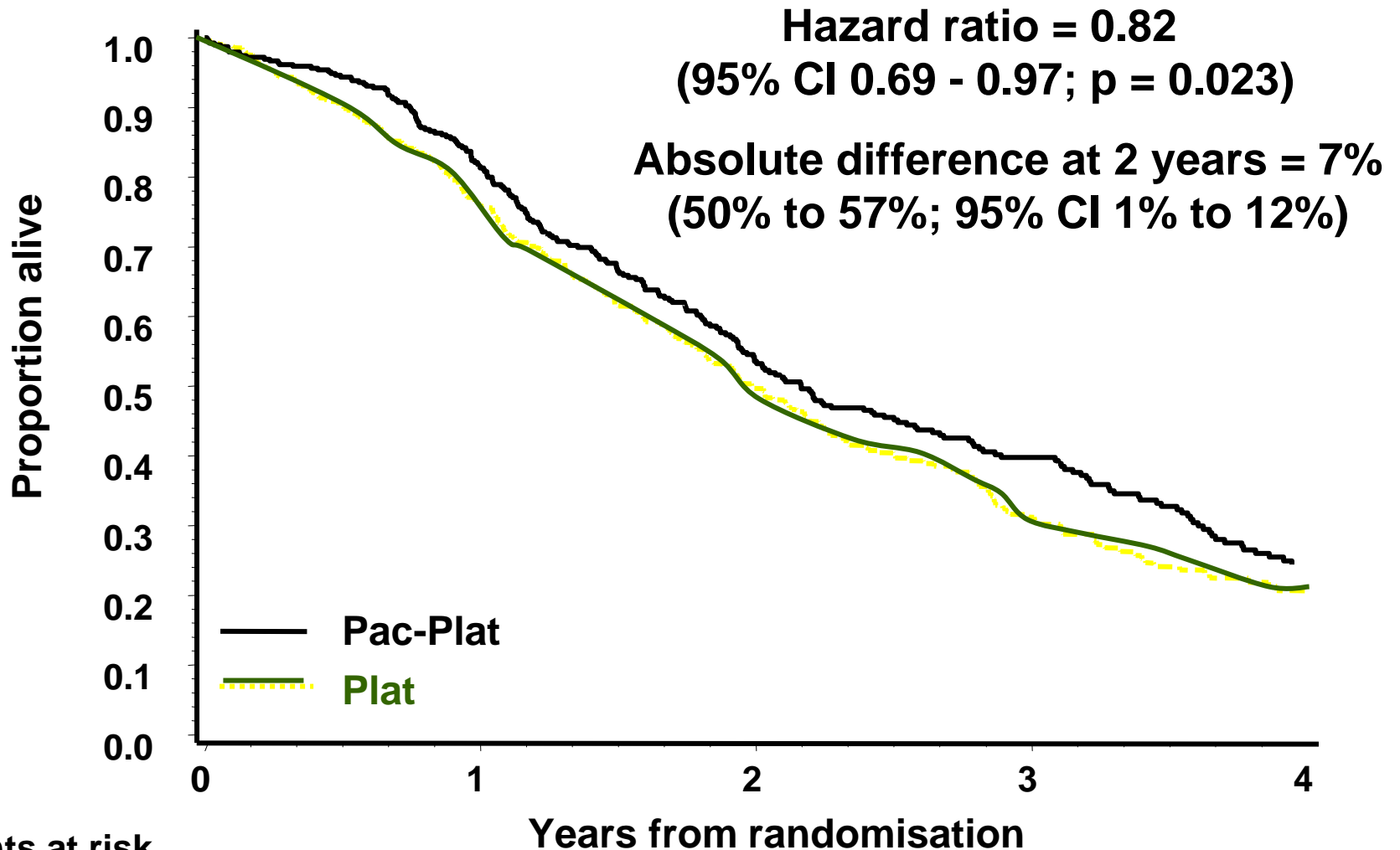
ICON4 PROGRESSION FREE SURVIVAL



Patients at risk

Pac-Plat	392	179	52	25	17
Plat	410	157	45	17	7

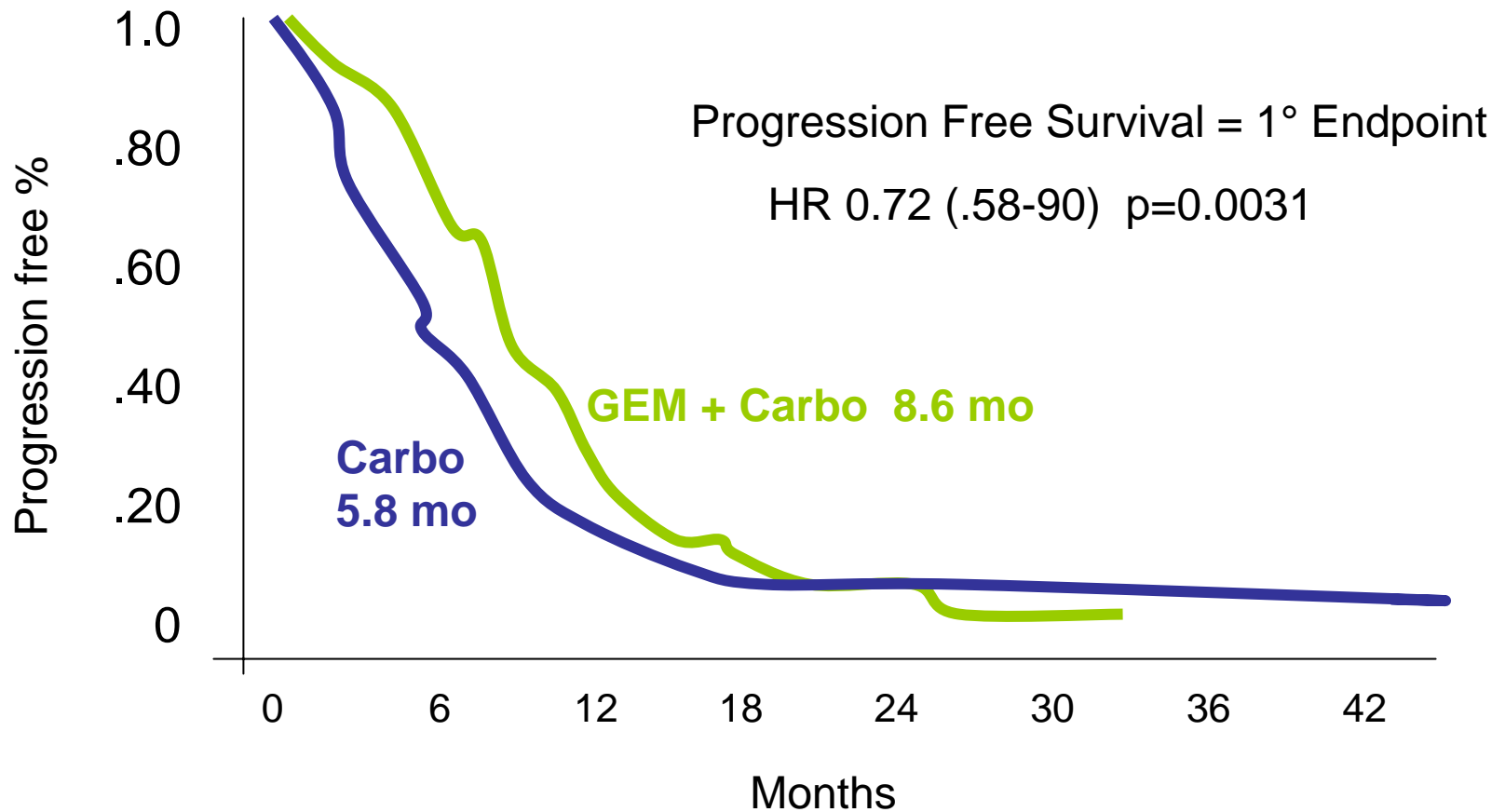
ICON4 Overall survival



Patients at risk

Pac-Plat	392	306	167	96	43
Plat	410	295	150	68	33

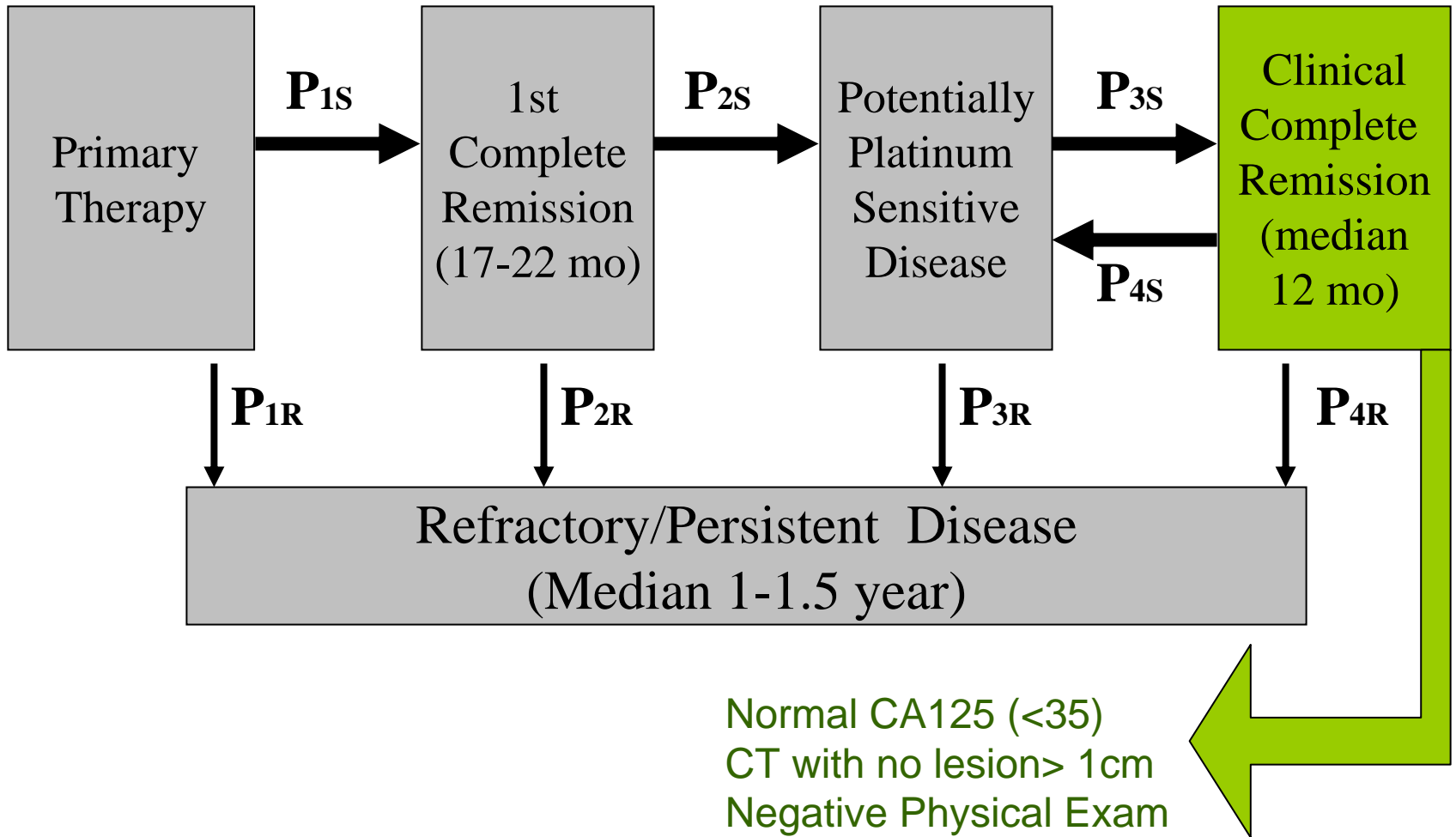
AGO: Carb vs Carb Paclitaxel



Commentary

- Only ICON4 is prospective with OS as primary endpoint
- The AGO trial is sized for PFS only
- The Gordon Trial is Subset Analysis
- None of the trials used CA125 as endpoint for progression

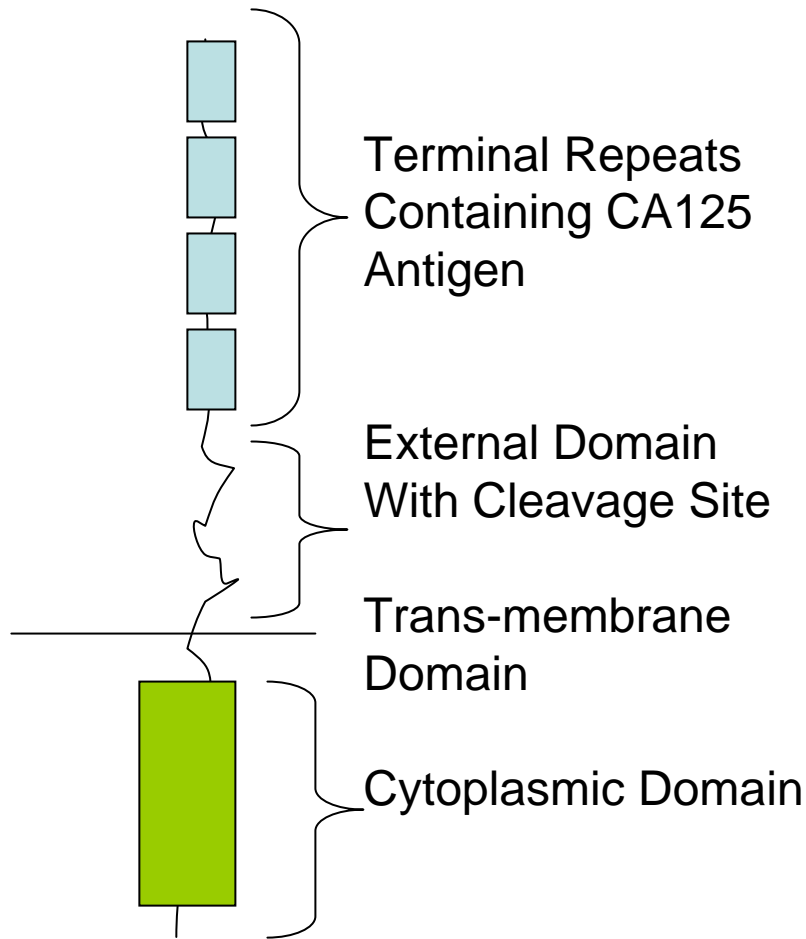
The relationship between PFS and OS is not proven in this setting



Second Remission Setting

- Eligibility
- Entry within 3 months
- NED (as defined above)
- CT q 3 months
- CA125 monthly[†]
- POD:
 - New lesion on CT scan
 - CA125 > 70 U/ml confirmed
- Trials To Date
- vaccines
- ACA 125[†]
- Imatinib
- GnRH + Andro Block

Biology of MUC16/CA125



- Largely unknown
 - Function
 - Triggers for secretion
 - Site of Cleavage
 - Binding Partners
 - MUC4
 - Fn of Cytoplasmic Domain
 - MUC1

Triggers for Ovcar 3 CA125 Release

