

Evolving Landscape of Diagnostics ***Unique Role for Novel Trial Designs***

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N-of-One: Is This the Future for Oncology Drug Development
Cancer Progress
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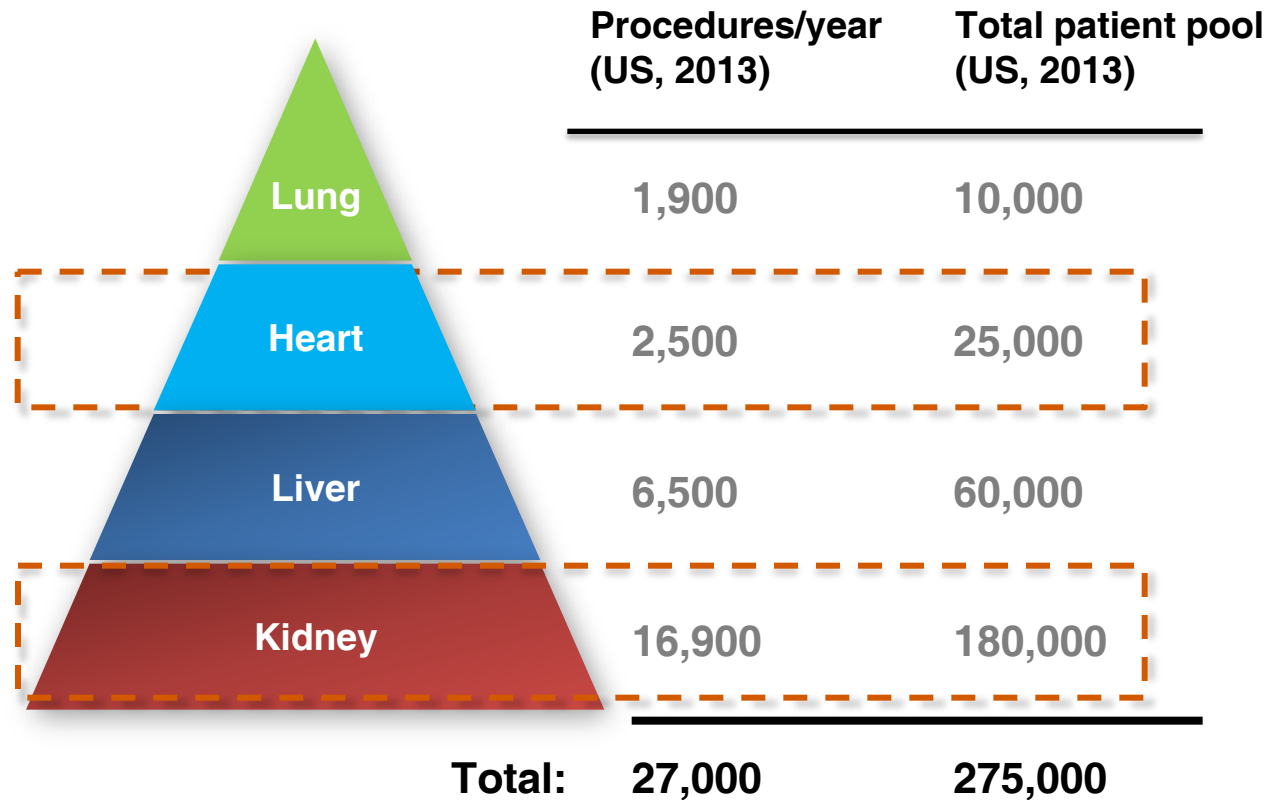
Context: Increased Cancer Risk in Organ Transplant Setting

- CareDx is a molecular diagnostics company focused on the discovery, development and commercialization of clinically differentiated, **high-value, personalized diagnostic surveillance solutions for transplant recipients**
- Organ transplant patients are at **significantly elevated de novo cancer risk** due to requisite chronic immunosuppressive therapy
 - Younger organ transplant patients are at even higher risk than older patients
- Organ transplant patients who develop cancer have been reported to **experience worse outcomes** than patients with cancer in general population

Cancer risk in U.S. transplant recipients

Cancer site *	Observed cases	Expected cases	SIR [†]	95% lower CI	95% upper CI	P-value
Infection-related malignancies						
NHL	1504	199.4	7.54	7.17	7.93	<0.0001
Nodal NHL	831	136.6	6.08	5.68	6.51	<0.0001
Extranodal NHL	673	62.8	10.72	9.93	11.56	<0.0001
Liver	930	80.5	11.56	10.83	12.33	<0.0001
Stomach	152	90.9	1.67	1.42	1.96	<0.0001
Kaposi sarcoma	120	2.0	61.46	50.95	73.49	<0.0001
Oropharynx including tonsil	106	52.8	2.01	1.64	2.43	<0.0001
Anus	90	15.4	5.84	4.70	7.18	<0.0001
Hodgkin lymphoma	85	23.7	3.58	2.86	4.43	<0.0001
Vulva	58	7.6	7.60	5.77	9.83	<0.0001
Cervix	45	43.6	1.03	0.75	1.38	0.88
Penis	22	5.3	4.13	2.59	6.26	<0.0001
Nasopharynx	8	8.3	0.96	0.42	1.90	1.00
Vagina	7	3.0	2.35	0.94	4.84	0.07
Infection-unrelated malignancies						
Lung	1344	682.8	1.97	1.86	2.08	<0.0001
Prostate	1039	1126.9	0.92	0.87	0.98	0.009
Kidney	752	161.8	4.65	4.32	4.99	<0.0001
Colorectum	627	504.9	1.24	1.15	1.34	<0.0001
Breast	481	567.9	0.85	0.77	0.93	0.0002
Melanoma	381	160.3	2.38	2.14	2.63	<0.0001
Thyroid	238	80.8	2.95	2.58	3.34	<0.0001
Urinary bladder	225	148.1	1.52	1.33	1.73	<0.0001
Skin (non-melanoma, non-epithelial)	184	13.3	13.85	11.92	16.00	<0.0001
Pancreas	157	107.3	1.46	1.24	1.71	<0.0001

Context: Post-Transplant Surveillance Unmet Clinical Need



- Challenging ROI for diagnostic trials
- Few treatment clinical trials now initiated in transplant space
- Modest transplant patient numbers for each organ
- Long term outcomes increasingly important requiring increased investment in trials

Changing Landscape of Companion Diagnostics

	Past State	Future State
Diagnostic test regulatory oversight	CMS CLIA service and FDA approved IVD product	FDA cleared / approved product
Regulatory evidence	RCT exclusively	RCT complemented with additional evidence approaches
Registries	Not used	Used
Adaptive trial design	Not used	Used
EMR	Not used	Used
n-of-one	Not used	Used
Reimbursement evidence	Clinical validity	Clinical utility (actionable)
Diagnostic valuation	Cost plus fee; test provider not involved in evidence	Value add to patient management; vendor responsible for evidence
Evidence	Binary	Staged licensing
Diagnostic testing	Insufficient tissue and excessively expensive	Sufficient tissue and cost-effective
Next Gen sequencing	Research-grade	Clinical-grade
'Follow on' Dx tests	Analytical validity with proficiency	TBD
Companion diagnostic	Single analyte : single drug	Multi-analyte : multi-drug
Computational analysis	On-premise	Cloud-based
Variant or mutation analysis	Laboratory-specific interpretation	Clinically validated community standards high quality databases