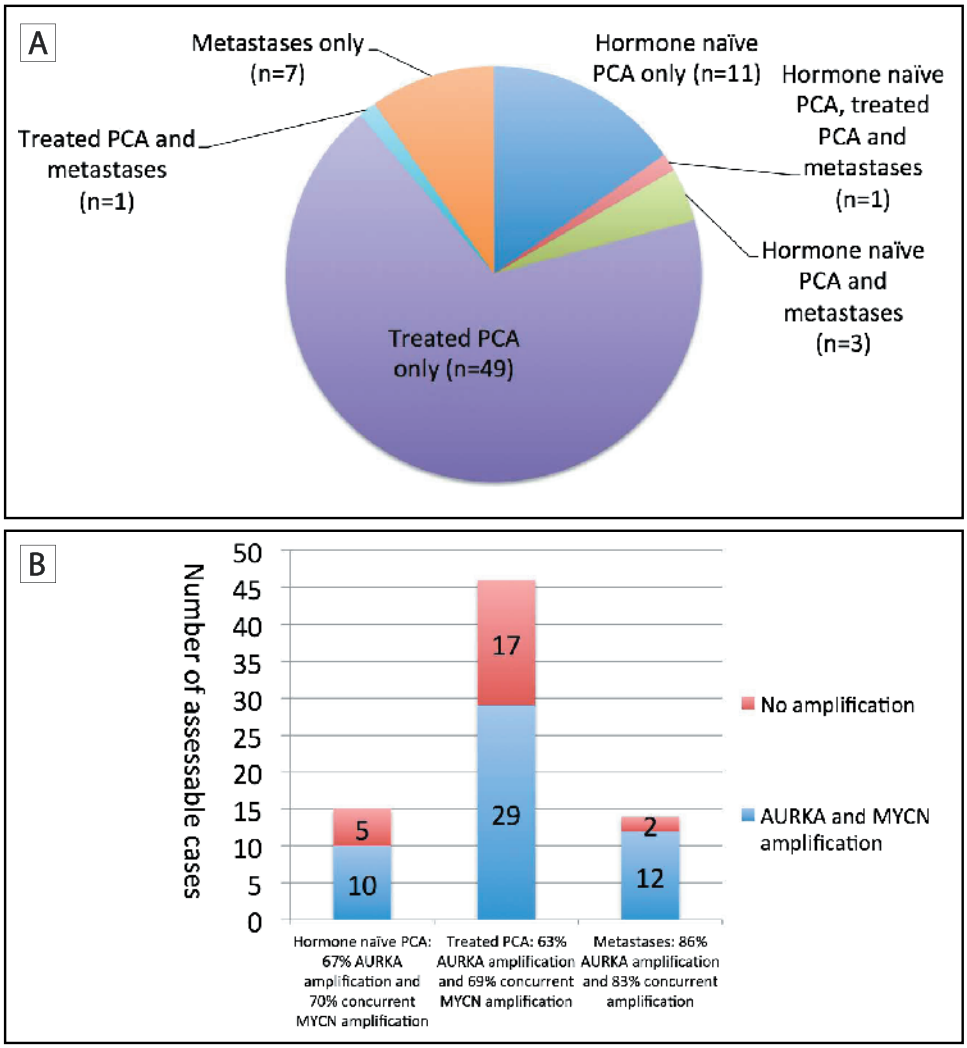

Figure W1. Summary of prostate cancer specimens interrogated for *AURKA* and *MYCN* gene amplifications in the current study. (A) Tumors from 72 patients at different stages of disease progression to t-NEPC were studied: 15 hormone naïve prostate cancers, 51 treated prostate cancer cases, and 15 metastases from 12 patients. Some patients had multiple specimens. (B) Results of *AURKA* and *MYCN* gene amplifications evaluated by FISH in assessable cases of hormone naïve PCA, treated PCA, and metastases.

Table W1. Clinicopathologic Characteristics, Treatment and Follow-up of Patients Who Developed t-NEPC.

Case	Site	Clinical Course	Time on Hormonal Therapy (years)	Age (years)	Survival (years)	Diagnosis	Pathology	FISH			
								ERG	PTEN	AURKA	NMYC
2	Retroperineal mass and bladder	RP 1992, XRT 1995, ADT 2000, anaplastic recurrence pelvic mass + RP lymph nodes (LN), low PSA (4 ng/ml); 2001—J591, estramustane, cytoxan, taxol, carboplatin-taxol, nizoral-adriamycn	2	76	10 (14 months since dx anaplastic)	Poorly diff AdenoCa NED	PCA in retroperineal mass and bladder from cysto/transrectal prostate biopsies; s/p RP and hormonal therapy and radiation	T	DEL	AMP	Polysomy
7	Prostate (autopsy case)	ADT only with suppressed PSA but rapidly developed widely met CRPC to LN, stomach, iliac fossa, bladder, bone with PSA (9 ng/ml), autopsy case	2	88 at dx, 90 at death	2	Poorly diff AdenoCa	PCA with treatment effect in prostate and multiple metastases from autopsy	T	DEL	AMP	AMP
8	Prostate (autopsy case)	RP 1997 (age 43), XRT, ADT, docetaxel, irinotecan, widely metastatic autopsy to liver, peritoneum, lung, LN, autopsy case	9	42 at dx, 56 at death	12	Poorly diff AdenoCa	PCA in prostate area and multiple metastases from autopsy	T + D	–	–	AMP
10	Prostate	RP, XRT, ADT, three to four lines chemotherapy	2	dx 64	13, three from mets, one from NEPC dx	AdenoCa	Primary PCA Gleason 7 (3 + 4) from biopsies	–	–	–	–
14	Prostate (metastatic disease)	Presented with metastatic disease 2009, PSA 33, prostate bx Gleason 4 + 4; developed CRPC 2010, ADT, MDV3100, docetaxel + radium-223	3	dx age 61	Alive	AdenoCa	Primary PCA Gleason 7 (4 + 3) from biopsies	T	–	–	–
16	Bladder Met/Prostate	RP 1990 for PSA 50, Gleason 4 + 3, 1/10 LN, ADT 1991→bladder recurrence 2010, PSA 0.03, elevated chromogranin 1617 and NSE 15	11	66 at dx, now 78	Alive	AdenoCa	PCA with treatment effect from TURB; positive PSMA and negative PSA, CGA, and SYP	–	DEL	AMP	AMP
17	Spinal Metastasis	RP 1999 for Gleason 4 + 4, XRT 2000, bone mets 2004, ADT, CRPC 2007, J591, docetaxel, abiraterone × 9 months, carboplatin-taxol, cord compression and brain mets 2011	7	dx age 56, mets age 61, death 68	12	AdenoCa met	Metastatic PCA to brain and spinal cord; positive PSMA and negative PSA	–	–	AMP	–
18	Spinal Metastasis	XRT + ADT 2004 for Gleason 5 + 5, PSA 26, ADT, CRPC 2006, docetaxel, J591	4	dx age 65, died age 69	4	Poorly diff AdenoCa	Metastatic PCA from spinal tumor; weakly positive for PSA	Polysomy	Homo Del	AMP	AMP
19	Prostate (metastatic disease)	ADT, cisplatin-etoposide, carboplatin-taxol, palliative XRT bone	1	56	2	Mixed small cell and 4 + 5	PCA Gleason 9 (4 + 5) with ductal features and focal small cell diff. from TURP; negative PSA, and positive focal CGA and diffuse NSE	T + D	DEL	Polysomy	–
20	Prostate (metastatic disease)	XRT for Gleason 4 + 3, multiple TURPS, ADT, bone mets, liver mets	4	dx age 67, NEPC age 77	10	Mixed (small cell + AdenoCa)	PCA Gleason 10 (5 + 5) and majority of tumor consisting of small cell undifferentiated variant (90%) from TURP; primary	del both 5′ signals	Homo Del	Polysomy	–

Table W1. (*continued*)

Case	Site	Clinical Course	Time on Hormonal Therapy (years)	Age (years)	Survival (years)	Diagnosis	Pathology	FISH			
								ERG	PTEN	AURKA	NMYC
21	Prostate (metastatic disease)	RP for Gleason 7 LN+ in 1996, ADT, LN/liver mets 1999 with TURP at that time t-NEPC, cisplatin-etoposide, carboplatin-taxol, pelvic RT	3	dx age 58, NEPC age 61	3	Small cell Ca	Small cell anaplastic carcinoma from TURP; negative PSA, CGA, SYP, and PAP	T	–	AMP	AMP
23	Prostate (metastatic disease)	RP 2006 for Gleason 5 + 4, 3/19 LN, mets 2006 with PSA 0.06, ADT, docetaxel, cisplatin-etoposide, J591, carboplatin-taxol	5	dx age 54	Alive	AdenoCa (3 + 3)	PCA Gleason 9 (5 + 4) from RP	T	–	AMP	AMP
24	Prostate (metastatic disease)	RP 2008 Gleason 4 + 3 pT3a, bone mets 2009, cord compression 2009 elevated chromogranin 191, NSE 23	1	59	1 diagnosis→death	AdenoCa (5)	PCA Gleason 9 (4 + 5) from RP	–	–	–	–
25	Prostate (metastatic disease)	XRT 2002 Gleason 8, ADT 2006, local recurrence 2009 NEPC, chromogranin >7000 NSE 65, cisplatin-etoposide, salvage RP 2010	4	dx 2002 age 62, death age 71	9 (14 months NEPC to death)	Small cell Ca	Undifferentiated NE carcinoma from prostate biopsies; strong CD56, moderate TTF-1; negative PSAP and PSMA	T + D	–	AMP	AMP
27	Prostate (metastatic disease)	RP, salvage XRT, intermittent ADT, R-CHOP (for lymphoma), pt later developed liver mets NEPC with elevated CEA	5	59	6	AdenoCa (4 + 3)	Primary PCA Gleason 7 (4 + 3); liver metastasis with NEPC	T + D	–	AMP	AMP
30	Pleural metastasis	XRT 1989, treated ADT 1990s, docetaxel, abiraterone—liver, lung, and pleura mets with low PSA (8 ng/ml), carboplatin-paclitaxel	10	dx age 71, NEPC age 81	22 from dx to death, 8 months from NEPC to death	Small cell Ca met	Small cell carcinoma	T + D, ploidy	–	AMP	AMP
74	Prostate (metastatic disease)	Intermittent ADT 1992, XRT, DES, docetaxel + CNTO, docetaxel + revlimid, ipilumimab *versus* placebo, cabazitaxel, then abiraterone. cytopenias despite dropping PSA, BM c/w NEPC, rapidly progressed and died in hospice 1 month later	10	dx 51, died 71	20	AdenoCa	Well-differentiated adenocarcinoma; TURP specimen, confirmed primary PCA Gleason 6 (3 + 3) and 8 (4 + 4) in biopsies from 1993, bone metastasis in 2011 with NEPC	T	Homo Del	AMP	AMP
75	Prostate and pelvic mass	XRT + ADT 2008 for Gleason 4 + 4; developed local recurrence 2011, NEPC 6.6 × 5.2 cm pelvic mass with local ext to bladder/colon, carboplatin/etoposide	4	dx 75	Alive	AdenoCa (4 + 4)	Primary PCA Gleason 8 (4 + 4) and 6 (3 + 3), biopsies	–	–	AMP	AMP

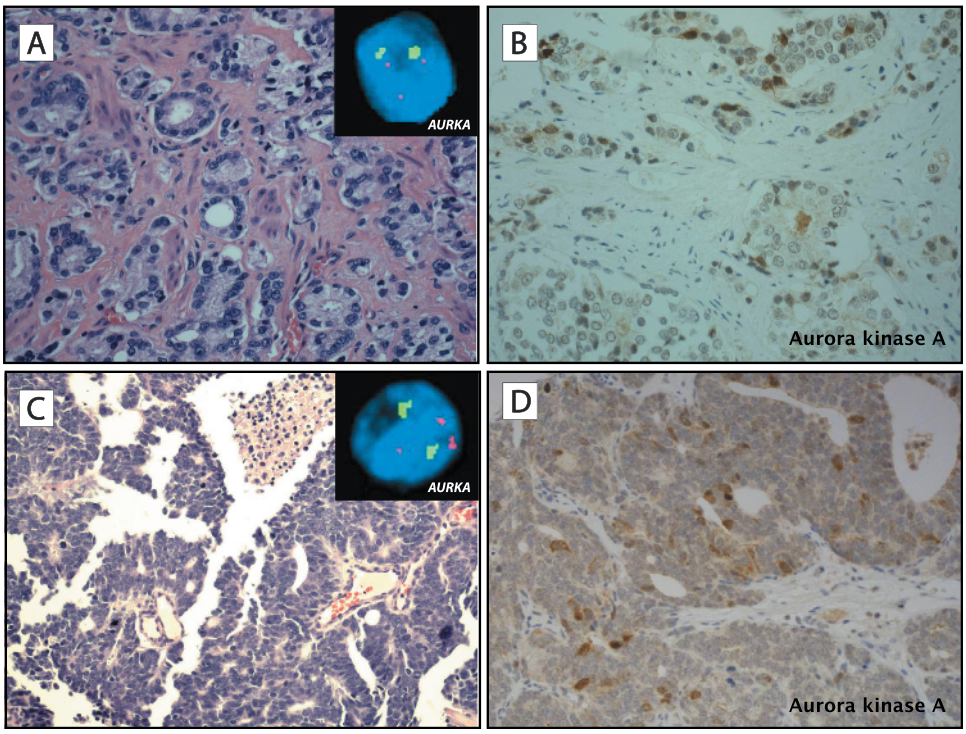

Figure W2. Aurora kinase A overexpression is present in primary PCA with *AURKA* amplification from patients who later developed t-NEPC. Aurora kinase A overexpression by IHC was detected in five of seven primary PCAs with *AURKA* gene amplification from patients who clinically develop t-NEPC. Illustrated here are two of such cases. (A) Primary prostatic adenocarcinoma, Gleason score 4 + 3 = 7 with *AURKA* amplification (inset) from a 59-year-old patient who, 6 years after initial diagnosis, developed t-NEPC. (B) Overexpression of Aurora kinase A is present. (C) Primary prostatic adenocarcinoma, Gleason score 5 + 4 = 9 with *AURKA* amplification (inset) from a 65-year-old patient who, 9 years after initial diagnosis, developed t-NEPC. (D) Overexpression of Aurora kinase A is present (H&E and IHC stains of A and B, original magnification, ×400; H&E and IHC stains of C and D, original magnification, ×200; FISH images, original magnification, ×600).