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Oncology

Literature Review and study overview

Chromogranin A for therapy monitoring of patients with prostate cancer

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Contents

Comprehensive analysis of serum chromogranin A and neuron-specific enolase levels in localized and castration-resistant prostate cancer

Authors

Szarvas, T., A. Csizmarik, T. Fazekas, A. Hüttl, P. Nyirády, B. Hadaschik, V. Grünwald, L. Püllen, Z. Jurányi, Z. Kocsis, S. F. Shariat, S. Sevcenco, A. Maj-Hes, and G. Kramer (2020). BJU Int 127(1): 44–55. (Szarvas, Csizmarik et al. 2020)

Rationale

Prognostic and therapy predictive value of the established neuroendocrine serum markers CgA and neuron-specific enolase (NSE) were evaluated in men with localized prostate cancer and men with metastatic castration resistant prostate cancer (mCRPC).

Methods

Serum samples of patients were analyzed in three treatment groups: radical prostatectomy (RPE) cohort (n = 157) with clinically localized and hormone naïve prostate cancer (PCA), a cohort with metastatic castration-resistant prostate cancer receiving first line docetaxel chemotherapy (mCRPC; n = 95)) and a cohort with mCRPC receiving hormonal therapy with abiraterone (ABI) or enzalutamide (ENZA; n = 143)).

Laboratory method

CgA II on Thermo Scientific™ B·R·A·H·M·S™ KRYPTOR™

Results

- Thermo Scientific B·R·A·H·M·S CgA II KRYPTOR levels are approximately 3-fold higher in patients with mCRPC (median = 140.4 ng/mL) compared to clinically localized and hormone naïve patients (median = 50.4 ng/mL).
- Cutoffs were optimized for B·R·A·H·M·S CgA II KRYPTOR to predict outcome (i.e. overall survival):

  a) > 168.0 ng/ml in patients treated with docetaxel chemotherapy (p = 0.041);

  b) > 81.2 ng/ml in patients treated with abiraterone or enzalutamide (p = 0.047).

- In the cohort treated with either abiraterone or enzalutamide > 50 % increases of CgA concentration were associated with an almost two-fold higher risk of death (HR = 1.76; p = 0.39). In the cohort with baseline CgA values above the upper limit of normal (ULN, CgA > 101.9), the risk was already more than two-fold higher starting at increases of > 20 % (HR = 2.13; p = 0.019); **Table 2**).
- An improved stratification model was developed by combining serum CgA at start of therapy together with CgA during follow up to predict outcome after treatment with abiraterone or enzalutamide (**Table 1**).

Key Conclusions

Serum CgA values are significantly elevated in progressed state and predicts outcome in patients with advanced disease.

Further increases of serum CgA levels during follow up of treatment with abiraterone or enzalutamide are associated with worse outcome (**Table 1**).

Table 1. Stratification model

Algorithm	Risk group
CgA ≤ 85 ng/ml at start of therapy	low risk = 95 % one-year survival rate
CgA > 85 ng/ml at therapy start/ no increase at 3 month	intermediate risk = 70 % one-year survival rate
CgA > 85 ng/ml at baseline/ increase > 20 % at 3 month	high risk = 43 % one-year survival rate

Table 2. The association of CgA values with the risk of mortality was analyzed by using cox univariable regression analysis in the ABI/ENZA (orange) cohorts. This was done for CgA changes over time in the whole cohort treated with ABI/ENZA (left) and in the subgroups with baseline (= at start of treatment) marker above the upper limit of normal (ULN: CgA > 101.9 ng/ml,right). This table was modified from Szarvas et al BJU Int. (2020). X-fold risk of death is expressed by hazard ratio (HR) and 95 % confidence intervals. p < 0.05 = statistical significance.

		Whole cohort				Subgroup with CgA above ULN			
	increase	**HR**	**95 % CI**		**p**	**HR**	**95 % CI**		**p**
3 months	any	0.826	0.579	1.179	0.294	0.924	0.49	1.742	0.808
	> 20 %	1.494	0.884	2.526	0.133	2.131	1.126	4.033	**0.019**
	> 50 %	1.759	1.027	3.011	**0.039**	2.083	1.087	3.988	**0.026**

Clinical features of neuroendocrine prostate cancer

Authors

Conteduca, V., C. Oromendia, K. W. Eng, R. Bareja, M. Sigouros, A. Molina, B. M. Faltas, A. Sboner, J. M. Mosquera, O. Elemento, D. M. Nanus, S. T. Tagawa, K. V. Ballman, and H. Beltran (2019). Eur J Cancer 121: 7–18. (Conteduca, Oromendia et al. 2019)

Rationale

NEPC is an aggressive variant of prostate cancer and can arise de novo or in patients previously treated with hormonal therapies for prostate adenocarcinoma as a mechanism of resistance. Defining clinical features of NEPC could help guide when to perform a biopsy to look for NEPC histologic transformation.

Methods

87 Patients with metastatic prostate cancer and a metastatic biopsy confirming pathologic features of NEPC were retrospectively identified at Weill Cornell Medicine (WCM) between 2004 and 2017. NEPC was defined by the presence of either pure small-cell carcinoma (by tumour morphology) or mixed histology with both adenocarcinoma and small-cell/neuroendocrine carcinoma present (mixed) using published criteria. Baseline, treatment and outcome data was reviewed.

Results

At the time of CRPC, median time from diagnosis of localised prostate cancer was 32.6 months (IQR: 17.0–74.3 months), median time from progression after ADT treatment was 8.3 months (IQR: 4.12–17.8 months), median PSA was 2.0 ng/ml (IQR: 0.16– 8.75), serum CGA was elevated above normal (> 95 ng/ml) in 85.7 % of cases (IQR: 177– 533). The authors did not find that PSA changed significantly from CRPC to t-NEPC. Nevertheless, patients who eventually developed t-NEPC had a progressive increase in serum neuroendocrine markers including CGA from initial diagnosis to CRPC (median = 42 ng/mL vs. 370 ng/mL; p = 0.029) and from CRPC to t-NEPC (median = 370 ng/mL vs. 476 ng/mL; p = 0.018, **Figure**).

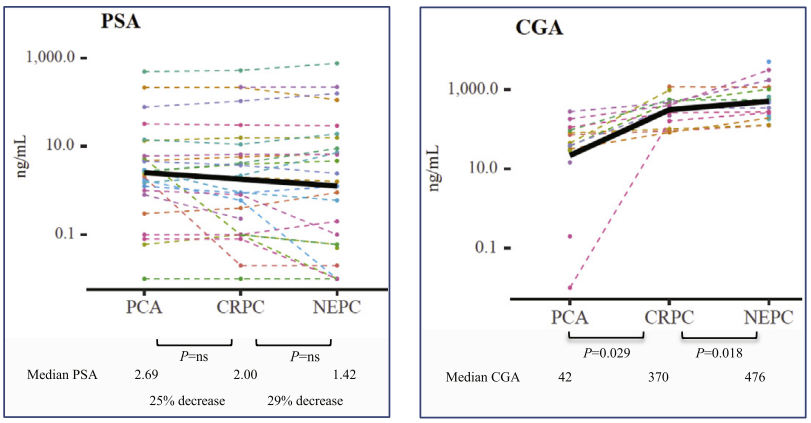

Figure 1. Exploratory CRPC adenocar-cinoma patterns of early transformation into NEPC. Laboratory values (PSA, CGA) at different time points from diagnosis of prostate cancer (PCA) through the castration-resistant state (CRPC) to the appearance of NEPC.

Key Conclusions

CgA levels increased in patients developing CRPC and NEPC when compared to baseline levels.

Serum Chromogranin A-based prognosis in metastatic castration-resistant prostate cancer

Authors

Giridhar, K. V., C. Sanhueza, D. W. Hillman, H. Alkhateeb, R. Carlson, W. Tan, B. A. Costello, F. Quevedo, L. Pagliaro and M. Kohli (2018). Prostate Cancer Prostatic Dis 21(3): 431–437. (Giridhar, Sanhueza et al. 2018)

Rationale

Determination of the prognostic value of serum Chromogranin A (CgA) in patients with metastatic castrate resistant prostate cancer (mCRPC).

Methods

Serum CgA was evaluated in a screening cohort (n = 200) and an independent validation cohort (n = 72) of men with mCRPC. Men receiving proton pump inhibitors and those with non-castrate levels of testosterone (> 50 ng/dl) were excluded.

Laboratory method

CgA on Thermo Scientific B·R·A·H·M·S KRYPTOR

Results

- Elevated CgA was defined as above upper limit of normal (> 93 ng/mL CgA).
- Screening cohort with mCRPC: Median serum CgA was 100.3 ng/mL (interquartile range 67–161.3), the mean was 184.8 ng/mL (standard deviation 396), and 34/200 (17 %) had an elevated CgA (above reference range of 225 ng/mL).
- In 81 men with a Gleason score of ≥ 8, elevated CgA was associated with shorter OS [HR 2.19, 95 %CI: 1.16 – 3.85, p = 0.02). CgA remained associated with overall survival after adjusting for PSA, Gleason score, time from diagnosis to study treatment and radiographic evidence of recurrent prostate cancer.
- Validation cohort with mCRPC: The median CgA was 90 ng/mL (IQ range 55–156), the mean was 174.7 ng/mL (standard deviation 280.2), and 31 (44 %) had a CgA above the reference range (> 93 ng/mL). Elevated serum CgA levels were associated with shorter OS (HR 1.91, 95 % CI 1.02– 3.67, p 0.043). In the sub-cohort of 36 patients with Gleason scores ≥ 8, the median OS in men with an elevated serum CgA was 6.9 months shorter compared to men with a normal serum CgA (12.0 months vs 18.9, log-rank p = 0.043).

Key Conclusions

- Elevated serum CgA was negatively associated with OS in men with mCRPC.
- Serum CgA represents a complementary prognostic biomarker.

Prospective Evaluation of Neuromediator Dynamics in Castration-Resistant Prostate Cancer Patients During Docetaxel

Authors

von Hardenberg, J., M. Schwartz, T. Werner, S. Fuxius, M. Muller, T. Frangenheim, C. Bolenz, C. Weiss and E. Heinrich (2017). Anticancer Res 37(9): 5117–5124. (von Hardenberg, Schwartz et al. 2017)

Rationale

Objective of the study was to evaluate temporal dynamics of CgA and NSE in serum of patients with mCRPC during docetaxel therapy.

Methods

Prospective observational study at six Germany institutions. Patients with histologically-confirmed adenocarcinoma, mCRPC (newly diagnosed or with progression after regimens with Abiraterone and/or Enzalutamide and/or Docetaxel) were included. In total 52 patients were evaluated.

Laboratory method

CgA on Thermo Scientific B·R·A·H·M·S KRYPTOR

Results

- Levels of CgA increased significantly from baseline compared to the 2nd and the 3rd blood withdrawal ($p = 0.0146$ and $p = 0.0330$).
- A total increase ≥ 100 % of the upper limit of normal (ULN) of CgA was observed in 11 patients.
- A high rise from baseline of CgA was associated with progression free survival (PFS; $p = 0.0369$) and high rise from baseline of CgA trended towards significance with overall survival (OS; $p = 0.0649$).

Key Conclusions

- Early high rise in CgA levels was associated with shorter PFS and trended towards significance with shorter OS.
- Early high rise of CgA should be further tested as a preselection tool for multi-core biopsy-sampling of metastases.

Influence of abiraterone acetate on neuroendocrine differentiation in chemotherapy-naive metastatic castration-resistant prostate cancer

Authors

Dong, B., L. Fan, Y. Wang, C. Chi, X. Ma, R. Wang, W. Cai, X. Shao, J. Pan, Y. Zhu, X. Shangguan, Z. Xin, J. Hu, S. Xie, X. Kang, L. Zhou and W. Xue (2017). Prostate 77(13): 1373–1380. (Dong, Fan et al. 2017)

Rationale

To determine the influence of abiraterone Acetate (AA) on neuroendocrine differentiation (NED) in patients with chemotherapy-naive metastatic castrationresistant prostate cancer (mCRPC).

Methods

Analysis of CgA in serum from 115 chemotherapy-naive mCRPC patients with decision for chemotherapy

Results

- Serum CgA levels of 56 patients (= 48.7 %) were above the upper limit of normal (ULN) before chemotherapy.
- The CgA decline and baseline normal CgA groups had much longer PSA PFS (medians: 14.34 vs 10.00 months, $p < 0.001$, and 14.23 vs 10.30 months, $p = 0.02$ respectively) and radiographic PFS (medians: 18.33 vs 11.37 months, $p < 0.001$, and 17.10 vs 12.07 months, $p = 0.03$ respectively).

Key Conclusions

- Circulating CgA seems to be an comprehensive and convenient indicator for revealing and quantifying NED in mCRPC.
- Serial CgA might help clinicians guide clinical treatment of mCRPC patients.

Chromogranin A and neuron-specific enolase serum levels as predictors of treatment outcome in patients with metastatic castration-resistant prostate cancer undergoing abiraterone therapy

Authors

Heck, M. M., M. A. Thaler, S. C. Schmid, A. K. Seitz, R. Tauber, H. Kubler, T. Maurer, M. Thalgott, G. Hatzichristodoulou, M. Hoppner, R. Nawroth, P. B. Luppa, J. E. Gschwend and M. Retz (2017). BJU Int 119(1): 30–37. (Heck, Thaler et al. 2017)

Rationale

The impact of elevated neuroendocrine serum markers on treatment outcome in patients with metastatic castration-resistant prostate cancer (mCRPC) undergoing treatment with abiraterone in a post-chemotherapy setting.

Methods

CgA and NSE and were determined in serum drawn before treatment with abiraterone from 45 patients with mCRPC.

Laboratory method

CgA on Thermo Scientific B·R·A·H·M·S KRYPTOR

Results

- Patients were stratified into low- (9 patients), intermediate- (18) or high-risk (18) groups according to elevation of none, one, or both neuroendocrine markers, respectively.
- Cut offs used for stratification: CgA = 85 ng/mL and NSE = 19 ng/mL.
- Risk groups correlated with decreasing median OS (median OS not reached vs 15.3 vs 6.6 months; $p < 0.001$), decreasing median clinical or radiographic PFS (8.3 vs 4.4 vs 2.7 months; $p = 0.001$) and decreasing median PSA-PFS (12.0 vs 3.2 vs 2.7 months; $p = 0.012$).

Key Conclusions

- High CgA and NSE correlated with shorter PSA-PFS, clinical or radiographic PFS, and OS.
- High CgA and NSE might indicate elevated risk of developing resistance under abiraterone treatment related to neuroendocrine differentiation.

Influence of abiraterone acetate on circulating neuromediators in chemotherapy-naive castration-resistant prostate cancer

Authors

von Hardenberg, J., M. Schwartz, T. Werner, S. Fuxius, M. Muller, C. Bolenz, C. Weiss and E. Heinrich (2016). Prostate 76(7): 613–619. (von Hardenberg, Schwartz et al. 2016)

Rationale

Assessment of serum CgA in patients with chemotherapy-naïve CRPC. The relation between NED and abiraterone treatment was investigated.

Methods

35 chemotherapy-naive CRPC patients with clinical or radiographic progression of disease (16 priory received Abiraterone Acetate).

Laboratory method

CgA on Thermo Scientific B·R·A·H·M·S KRYPTOR

Results

- Serum CgA values were above the upper limit of normal (ULN) in 20 (57.1 %) patients.
- In univariate analysis, lymph node metastasis (p = 0.014), was significantly associated with upregulated circulating CgA levels. On multivariate Cox regression analysis, duration of ADT (p = 0.0101) but also proton pump inhibitors (p = 0.030) were significantly correlated with CgA levels above the upper limit of normal.

Key Conclusions

- Intake of proton pump inhibitors influences CgA and stop of intake might be considered when analyzing CgA.
- Neuromediators were frequently overexpressed after treatment with AA in chemotherapy-naïve CRPC.
- The study gives an insight into the simultaneous expression of neuromediators in chemotherapy-naïve CRPC and underlines the influence of the duration of ADT as key driver of NED.

Chromogranin A predicts outcome in prostate cancer patients treated with abiraterone

Authors

Burgio, S. L., V. Conteduca, C. Menna, E. Carretta, L. Rossi, E. Bianchi, B. Kopf, F. Fabbri, D. Amadori and U. De Giorgi (2014).Endocr Relat Cancer 21(3): 487–493. (Burgio, Conteduca et al. 2014)

Rationale

Evaluation of the Chromogranin A (CgA) baseline value as predictor of clinical outcome in patients with metastatic castration-resistant prostate cancer (CRPC) treated with abiraterone 1000 mg abiraterone per day.

Methods

48 consecutive metastatic CRPC patients progressing after docetaxel chemotherapy and decision to start abiraterone treatment.

Results

- CgA levels more than three times the upper normal limit (UNL) predicted an early radiological progressive disease in eight of 11 cases (73 %).
- Patients were stratified into three groups: CgA: < 120 ng/ml (group A, n = 16), 120 – 360 (group B, n = 16), >/= 360 ng/ml (group C, n = 16). The median progressionfree survival (PFS) among the CgA groups A, B, and C was 9.2, 9.2, and 4.8 months respectively, p = 0.0459.
- In the multivariate analysis, PSA response rate (nonresponsive vs responsive) and CgA levels were predictors of PFS (p = 0.0002 and p = 0,0047 respectively).
- CgA was predictive for CT (imaging-based) response at 3 month (complete response, partial response and stable disease vs progressive disease) with an AUC = 0.81.

Key Conclusions

- Elevated plasma CgA levels are frequently observed in CRPC patients after docetaxel.
- A plasma CgA level more than three times the UNL predicted PFS and showed a trend vs OS prediction, independently from PSA decline, in CRPC patients treated with abiraterone.

Distribution of high Chromogranin A serum levels in patients with nonmetastatic and metastatic prostate adenocarcinoma

Authors

Sciarra, A., F. Di Silverio, A. M. Autran, S. Salciccia, A. Gentilucci, A. Alfarone and V. Gentile (2009). Urol Int 82(2): 147–151. (Sciarra, Di Silverio et al. 2009)

Rationale

To evaluate the incidence of elevated serum levels of serum Chromogranin A (CgA) (as marker of neuroendocrine activity) in nonmetastatic and metastatic prostate cancer populations.

Methods

264 consecutive men with nonmetastatic prostate adenocarcinoma considered for radical prostatectomy (group 1) and 89 consecutive men with metastatic prostate adenocarcinoma (group 2) represented our population.

Results

- Group 1 (nmPC): CgA levels were in 35.0 % of cases > 60 ng/ml and in 6.4 % of cases > 90 ng/ml.
- Group 2 (mPC): CgA levels were in 100 % of cases > 60 ng/ml and in 69.7 % of cases > 90 ng/ml.
- Odds ratios (OR) for CgA level > 60 and > 90 ng/ml significantly increased from nonmetastatic to metastatic cases (p = 0.0001) → OR = 67.510 (23.182– 94.90) and = 33.364 (17.110 – 65.05) respectively.

Key Conclusions

A significant incidence of elevated serum levels of CgA either in nonmetastatic (using 60 ng/ml as cut-off) or in metastatic (using 90 ng/ml as cut-off) prostate adenocarcinoma cases is decribed.

Chromogranin A expression in patients with hormone naive prostate cancer predicts the development of hormone refractory disease

Authors

Berruti, A., A. Mosca, F. Porpiglia, E. Bollito, M. Tucci, F. Vana, C. Cracco, M. Torta, L. Russo, S. Cappia, A. Saini, A. Angeli, M. Papotti, R. M. Scarpa and L. Dogliotti (2007). J Urol 178(3 Pt 1): 838–843; quiz 1129. (Berruti, Mosca et al. 2007)

Rationale

The primary aim was to evaluate the value of tissue CgA to function as a biomarker in predicting the development of hormone refractory disease. Secondary aims were evaluating the prognostic role of CgA immunohistochemical detection, and the predictive and prognostic roles of increased plasma CgA levels at baseline and during androgen deprivation therapy.

Methods

175 patient were included with CgA measured. The study was monocentric and the inclusion criteria for the study were histologically proven adenocarcinoma of the prostate, intermediate to high risk of disease progression according to NCCN guidelines, i.e. T2b stage or more, or Gleason score 7 or more, or serum PSA 10 ng/ml or greater, or eligibility for androgen deprivation therapy.

Results

- Concordance of plasma CgA and tumor tissue CgA status was seen in 105 of 175 patients (60 %) while 52 patients (30 %) had positive immunohistochemistry but negative plasma levels and reverse was observed in 18 (10 %). Increased plasma CgA was observed in 18 of 101 (18 %) with immunohistochemically negative CgA, and in 16 of 65 (25 %) and 6 of 9 (67 %) patients with CgA positive tumors in less than 30 % or 30 % or more cells, respectively (chi-square test for trend p = 0.006).
- Serum CgA at baseline (HR 3.0, 95 % CI 1.8 – 5.2), after 1 year (HR 5.8, 95 % CI 3.1–10.1) and 2 years (HR 3.5, 95 % CI 1.6 –7.6) was predictive of hormone refractory risk and confirmed relation of tissue CgA with outcome.

Key Conclusions

- CgA detected in plasma or in tumor biopsies of patients with prostate cancer on androgen deprivation therapy are independent predictive parameters for earlier onset of hormone refractory disease and death.
- The predictive significance of plasma CgA is maintained over time.

Circulating Chromogranin A and hormone refractory prostate cancer chemotherapy

Authors

Cabrespine, A., L. Guy, F. Gachon, H. Cure, P. Chollet and J. O. Bay (2006). J Urol 175(4): 1347–1352. (Cabrespine, Guy et al. 2006)

Rationale

To better evaluate the interest of circulating CgA in terms of prevalence, chemo-therapy response and survival in HRPC we analyzed 39 patients who received 2 types of chemotherapy.

Methods

Serum CgA was analyzed in 39 patients treated for hormone refractory prostate cancer (HRPC) with paclitaxel or carboplatin (175 mg/m2 paclitaxel and carboplatin dosed to an area under the on day 1 of every 3-week cycle).

Results

- 45 % of patients with HRPC showed increased serum CgA. Local radiotherapy and the duration of hormonal therapy were independent factors that influenced CgA. Three classes of CgA during chemotherapy (25 % ≥ decrease, stability, and 25 % ≥ increase) correlated with measurable disease (complete + partial response vs stability + progression).

Key Conclusions

- The results of the study support the theory that circulating CgA may be predictive of the chemotherapy response in patients with HRPC.
- CgA level variations during treatment offer information complementary toPSA for following the chemotherapy response.

Elevated serum Chromogranin A precedes prostate-specific antigen elevation and predicts failure of androgen deprivation therapy in patients with advanced prostate cancer

Authors

Chuang, C. K., T. L. Wu, K. C. Tsao and S. K. Liao (2003). J Formos Med Assoc 102(7): 480–485. (Chuang, Wu et al. 2003)

Rationale

This study examined whether the neuroendocrine biomarker CgA could be used as prognostic marker in prostate cancer and whether expression of CgA appears earlier than the changes of PSA in the development of HRPC in patients under ADT.

Methods

Patients with locally advanced (n = 20) or metastatic (n = 70) PC receiving ADT were enrolled. Serum CgA was assessed before ADT and every 3 months during ADT treatment. The median follow-up was 35 months and at least 3 serum samples were obtained during ADT in 78 patients

Results

- 36 (46.2 %)of patients had no PSA re-elevation (< 4 ng/mL) and their CgA remained low (< 84.6 ng/mL). 17 patients (21.8 %) also had low PSA (< 4.0 ng/mL) but had progressively increasing CgA, while 25 patients (32 %) developed HRPC.
- Of the 25 patients with HRPC, 17 showed progressive elevation of serum CgA (> 100 ng/mL). CgA elevations were followed by PSA elevation after a median interval of 10 month. Serum CgA elevations were therefore detected earlier than PSA elevations in 21,8 % of 78 patients.

Key Conclusions

- Elevations of serum CgA preceded elevations of PSA in metastatic prostate cancer patients and/or in patients with high serum PSA who developed hormone resistance.
- Elevated CgA predicted the development of HRPC.

Acquired neuroendocrine-positivity during maximal androgen blockade in prostate cancer patients

Authors

Tarle, M., M. Z. Ahel and K. Kovacic (2002). Anticancer Res 22(4): 2525–2529. (Tarle, Ahel et al. 2002)

Rationale

Aims were to evaluate the influence of maximum androgen blockade on CgA positivity over time.

Methods

Patiens were n = 79 referred to maximal androgen blockade and n = 24 Stage C-D1 prostate cancer patients without therapy through their own choice and n = 20 controls (BPH). Maximal androgen blockade was done with LH-RH analogue and flutamide (750 mg daily dose).

Serum PSA, % FPSA and CgA concentrations were measured at three-month intervals and bone scans were performed 1–2 times during the overall monitoring period. CgA was followed-up for 15 months.

Results

- During the last six months of monitoring, the acquired CgA-positivity was statistically significant in treated patients when compared to the untreated group ($p < 0.001$, see **Figure 1**).
- Bone metastases were found in 38 % of CgA-positive prostate cancer patients (regardless of the therapy status) and in only 6 % of studied patients with a steady normal serum CgA concentration.

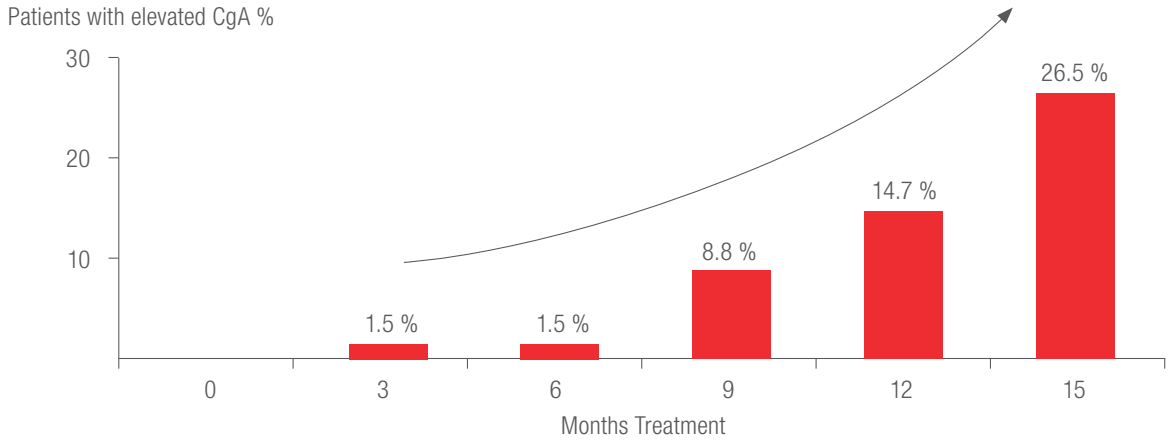

Figure 1. Percentage of patients with acquired CgA positivity in the group with hormonal treatment.

Key Conclusions

- Authors advocate the assessment of serum CgA at 3-months intervals during hormonal therapy.

Serum Chromogranin A in monitoring metastatic prostate cancer patients

Authors

Tarle, M. (1999). Anticancer Res 19(6C): 5663–5666

Rationale

This study was undertaken to delineate the role of serum CgA concentrations as a possible prognosticator of hormonal and chemo hormonal treatment.

Methods

Serum CgA was evaluated in 24 responders and 14 non responders to maximum androgen blockade (Flutamide 750 mg daily and LH-RH analogs) and chemo hormonal treatment (Estracyt). 12 patients with BPH were included as controls.

Results

- In responders and nonresponders to maximum androgen blockade mean +-SD CgA levels (ng/ml) were 39.5 +-18.3 (7.6 –78.4) and 214.8 +-250.3 (9.9 –1084.3) respectively.
- In responders (19) and nonresponders (12) to Estracyt, mean CgA +-SD (ng/ml) was 47.6 +/-22.7 (4.4 –101.2) and 366.7 +/-291.4 (82.0 – 925.7) respectively. Osseous metastates were detected in all patients. Cessation of Estracyt therapy in 4 of 14 responders caused sharp elevations of CgA levels.

Key Conclusions

- It is concluded that estracyt may control activity of CgA positive structures.
- The authors advocate serial assessment of serum CgA together with PSA for monitoring patients receiving hormonal therapy.

References

Berruti, A., A. Mosca, F. Porpiglia, E. Bollito, M. Tucci, F. Vana, C. Cracco, M. Torta, L. Russo, S. Cappia, A. Saini, A. Angeli, M. Papotti, R. M. Scarpa and L. Dogliotti (2007). "Chromogranin A expression in patients with hormone naive prostate cancer predicts the development of hormone refractory disease." J Urol 178(3 Pt 1): 838–843; quiz 1129.

Burgio, S. L., V. Conteduca, C. Menna, E. Carretta, L. Rossi, E. Bianchi, B. Kopf, F. Fabbri, D. Amadori and U. De Giorgi (2014). "Chromogranin A predicts outcome in prostate cancer patients treated with abiraterone." Endocr Relat Cancer 21(3): 487–493.

Cabrespine, A., L. Guy, F. Gachon, H. Cure, P. Chollet and J. O. Bay (2006). "Circulating Chromogranin A and hormone refractory prostate cancer chemotherapy." J Urol 175(4): 1347–1352.

Chuang, C. K., T. L. Wu, K. C. Tsao and S. K. Liao (2003). "Elevated serum chromogranin A precedes prostate-specific antigen elevation and predicts failure of androgen deprivation therapy in patients with advanced prostate cancer." J Formos Med Assoc 102(7): 480–485.

Conteduca, V., C. Oromendia, K. W. Eng, R. Bareja, M. Sigouros, A. Molina, B. M. Faltas, A. Sboner, J. M. Mosquera, O. Elemento, D. M. Nanus, S. T. Tagawa, K. V. Ballman, and H. Beltran (2019). „Clinical freatures of neuroendocrine prostata cancer." Eur J Cancer 121: 7–18.

Dong, B., L. Fan, Y. Wang, C. Chi, X. Ma, R. Wang, W. Cai, X. Shao, J. Pan, Y. Zhu, X. Shangguan, Z. Xin, J. Hu, S. Xie, X. Kang, L. Zhou and W. Xue (2017). "Influence of abiraterone acetate on neuroendocrine differentiation in chemotherapy-naive metastatic castration-resistant prostate cancer." Prostate 77(13): 1373–1380.

Giridhar, K. V., C. Sanhueza, D. W. Hillman, H. Alkhateeb, R. Carlson, W. Tan, B. A. Costello, F. Quevedo, L. Pagliaro and M. Kohli (2018). "Serum Chromogranin-A-based prognosis in metastatic castration-resistant prostate cancer." Prostate Cancer Prostatic Dis 21(3): 431–437.

Heck, M. M., M. A. Thaler, S. C. Schmid, A. K. Seitz, R. Tauber, H. Kubler, T. Maurer, M. Thalgott, G. Hatzichristodoulou, M. Hoppner, R. Nawroth, P. B. Luppa, J. E. Gschwend and M. Retz (2017). "Chromogranin A and neurone-specific enolase serum levels as predictors of treatment outcome in patients with metastatic castration-resistant prostate cancer undergoing abiraterone therapy." BJU Int 119(1): 30–37.

Sciarra, A., F. Di Silverio, A. M. Autran, S. Salciccia, A. Gentilucci, A. Alfarone and V. Gentile (2009). "Distribution of high Chromogranin A serum levels in patients with nonmetastatic and metastatic prostate adenocarcinoma." Urol Int 82(2): 147–151.

Szarvas, T., A. Csizmarik, T. Fazekas, A. Hüttl, P. Nyirády, B. Hadaschik, V. Grünwald, L. Püllen, Z. Jurányi, Z. Kocsis, S. F. Shariat, S. Sevcenco, A. Maj-Hes, and G. Kramer (2020). „Comprehensive analysis of serum chromogranin A and neuron-specific enolase levels in localized and castration-resistent prostata cancer." BJU Int 127(1): 44–55.

Tarle, M., M. Z. Ahel and K. Kovacic (2002). "Acquired neuroendocrine-positivity during maximal androgen blockade in prostate cancer patients." Anticancer Res 22(4): 2525–2529.

Tarle, M. (1999). "Serum Choromogranin A in monitoring metastatic prostate cancer patients." Anticancer Res 19(6C): 5663–5666.

von Hardenberg, J., M. Schwartz, T. Werner, S. Fuxius, M. Muller, T. Frangenheim, C. Bolenz, C. Weiss and E. Heinrich (2017). "Prospective Evaluation of Neuromediator Dynamics in Castration-Resistant Prostate Cancer Patients During Docetaxel." Anticancer Res 37(9): 5117–5124.

von Hardenberg, J., M. Schwartz, T. Werner, S. Fuxius, M. Muller, C. Bolenz, C. Weiss and E. Heinrich (2016). "Influence of abiraterone acetate on circulating neuromediators in chemotherapy-naive castration-resistant prostate cancer." Prostate 76(7): 613–619.

Abbreviations

AA = Abiraterone Acetate

ADT = Androgen Deprivation Therapy

BPH = Benign Prostate Hyperplasia

CgA = Chromogranin A

CRPC = Castration Resistant Prostate Cancer

HRPC = Hormone Refractory Prostate Cancer

LH-RH = Luteinizing Hormone-Releasing Hormone

mCRPC = metastatic Castration Resistant Prostate Cancer

NED = NeuroEndocrine Differentiation

mPC = metastatic Prostate Cancer

nmPC = non-metastatic Prostate Cancer

NSE = Neuron-Specific Enolase

PFS = Progression Free Survival

PSA = Prostate-Specific Antigen

UNL = Upper Normal Limit

OR = Odd Ratio

OS = Overall Survival

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