A Phase 2 Pharmacodynamic Study of Pre-operative Figitumumab in Patients with Localized Prostate Cancer

Kim N. Chi¹,², Martin E. Gleave¹, Ladan Fazli¹, S. Larry Goldenberg¹, Alan So¹, Christian Kollmannsberger¹,², Nevin Murray², Anna Tinker², Michael Pollak³

Vancouver Prostate Centre, Vancouver, Canada; BC Cancer Agency, Vancouver, Canada; McGill University, Montreal, Canada

Corresponding author: Kim N. Chi, BC Cancer Agency, 600 West 10th Avenue, Vancouver, British Columbia, V5Z 4E6, Canada, Phone: 604-877-6000, Fax 604-877-0585, e-mail: kchi@bccancer.bc.ca

Supported by a grant-in-aid from Pfizer

Running Head: A pre-operative study of figitumumab in prostate cancer

Key Words: Prostate cancer, Insulin-Like Growth Factor I Receptor, Androgen Receptor, Pre-operative, Phase II Clinical Trial
STATEMENT OF TRANSLATIONAL RELEVANCE

This study of pre-operative administration of single-agent figitumumab, an insulin-like growth factor 1 receptor (IGF-IR) antibody, to patients with prostate cancer undergoing prostatectomy demonstrates biologic activity with decreased IGF-IR expression in prostate cancers. This effect was also associated with a decrease in prostate cancer androgen receptor expression and a PSA decline in the majority of patients. These novel data support the hypothesized role of the importance of IGF signalling in prostate cancer development and progression and justifies further clinical trials targeting this pathway.
ABSTRACT

Purpose: Activation of the insulin-like growth factor 1 receptor (IGF-IR) is implicated in prostate cancer development and progression. This study evaluated biologic and clinical effects of figitumumab, a fully human monoclonal IGF-IR antibody, in patients with localized prostate cancer.

Patients and Methods: Eligible patients received figitumumab 20 mg/kg intravenously every 3 weeks for 3 cycles followed by prostatectomy. The primary endpoint was IGF-IR expression inhibition as assessed by immunohistochemistry.

Results: Sixteen patients were accrued. Median age was 63 years, median PSA was 7.2 μg/L (range 2.5-35), clinical stage was T1 in 4 patients and T2 in 12 patients, Gleason score ≤7 or >7 in 15 and 1 patients. Two patients received only 1 cycle (patient choice and grade 3 hyperglycemia). A PSA decline from baseline of ≥25% and ≥50% occurred in 15 (94%) and 5 (31%) of patients. Mean figitumumab concentration was 350.4 μg/ml (26.3-492.8) in plasma and 51.3 μg/g (27.4-79.6) in prostate tissue. Compared to pre-treatment biopsies, IGF-IR expression decreased in the prostatectomy specimens in 14 of 16 patients. The mean IGF-IR immunohistochemistry visual score was 2.1 (SD=0.6) in biopsy and 1.1 (SD=0.5) in prostatectomy specimens (P<0.0001). Androgen receptor expression was also decreased and there was a trend for a decrease in downstream IGF-IR signalling components.

Conclusions: Figitumumab is biologically active in prostate cancer. PSA declines in treatment naïve patients were observed, potentially mediated by IGF-IR effects on
androgen receptor expression. These results support the clinical relevance of IGF-IR signalling in prostate cancer and justify further clinical trials.
INTRODUCTION

The insulin-like growth factor (IGF) axis is composed of 2 peptide growth factors (IGF-I and -II), 2 transmembrane receptors (IGF-IR and -IIR), 6 IGF binding proteins (IGFBP-1 to -6), and IGFBP proteases. IGFs are synthesized primarily in the liver and have effects on protein and carbohydrate metabolism, but also regulate cellular processes of proliferation, differentiation and apoptosis (1). These later attributes have resulted in the IGF axis being associated with a critical role in the development of a number of malignancies including prostate cancer (2). IGF-IR is a transmembrane receptor tyrosine kinase that is widely expressed in human tissues. Binding of IGF ligands induces conformational changes of IGF-IR and activation of its intrinsic intracellular tyrosine kinase activity. The activated receptor induces recruitment of the insulin receptor substrates (IRS) 1 and 2, which in turn activates the mitogen-activated protein kinase (MAPKinase) and the phosphotidylinositol 3-kinase (PI3K)/Akt intracellular signalling pathways, leading to cellular proliferation and apoptosis inhibition.

High blood concentrations of IGF-I has been associated with a risk of prostate cancer in meta-regression analysis (3), and high plasma IGF-I and low IGFBP-3 has been associated with more advanced stages of prostate cancer (4, 5). In human primary prostate cancers, IGF-IR, IGF-I and -II have all been reported to be increasingly expressed compared to normal prostate tissue (6-8), and is also increased in advanced and metastatic disease (9, 10). In the TRAMP model, prostate cancer incidence is substantially reduced in IGF-I deficient mice, whereas organ-specific overexpression of IGF-IR increased prostate neoplasia (11). In preclinical studies, the IGF axis appears to
be upregulated in bone metastases (12) and IGF-I has been demonstrated to accelerate
tumour growth (13), promote migration through PI3K/AKT (14), and be involved with
angiogenesis through vascular endothelial growth factor (15). An increasing body of
evidence has linked activation of the IGF axis with castrate resistant progression of
prostate cancer including via ligand independent activation of the androgen receptor
(16) and increases in IGF-I (17), IGF-IR (10), IGFBP-2 (18), and IGFBP-5 (19).

Thus, targeting the IGF axis is an attractive concept as a treatment for prostate
cancer. Pre-clinical studies have supported this approach using a variety of IGF
pathway inhibitors (20-22). In both castrate sensitive and resistant prostate cancer
models, activity has been observed with IGF-IR specific monoclonal antibodies which
induced tumor cell apoptosis, cell cycle arrest, and down-regulation of ligand-
independent, androgen-regulated gene expression (23).

Figitumumab is a fully human IgG2 antibody with high affinity for the IGF-IR.
Figitumumab induces IGF-IR down-regulation by promoting receptor internalization and
degradation. No figitumumab related dose limiting toxicities were identified at doses up
to 20 mg/kg in phase I studies and dose-dependent IGF-IR downregulation on
granulocytes and increases in circulating IGF-I have been observed (24, 25). We
undertook this pre-operative study to evaluate the effects of figitumumab in prostate
cancer cells directly. Treatment of men with figitumumab prior to surgery permits
evaluation of the prostatectomy specimens for changes in expression of IGF-IR and
related proteins allowing for proof of principle determination of biologic activity,
ascertainment of figitumumab concentrations within target tissues, and gain insights into
the downstream effects of IGF-IR inhibition and IGF biology in human prostate cancer.
PATIENTS AND METHODS

Eligibility Criteria

To be eligible, patients had to have biopsy confirmed adenocarcinoma of the prostate and previously untreated, with radical prostatectomy already decided as the planned primary treatment. Patients had to have a minimum of 2 positive biopsies and at least one of the following: serum prostate-specific antigen (PSA) > 10 ug/L, Gleason score 7-10, and/or Gleason score 6 cancer and ≥ 3 biopsies positive. Other inclusion criteria were an Eastern cooperative oncology group performance status 0-1, white blood cell count of ≥ 3.0 x 10^9/L, hemoglobin ≥ 100 g/L, platelets ≥ 100 x 10^9/L, and normal serum aspartate aminotransferase (AST), alanine transaminase (ALT), total bilirubin and creatinine. Patients on heparin or coumadin anticoagulation were ineligible. The study was approved by the institutional review board and all patients provided written informed consent.

Treatment and Follow-Up Plan

Figitumumab 20 mg/kg was delivered as a 2.5-hour intravenous infusion. Each course of treatment was composed of 3 injections of figitumumab given every 21 (+/- 3) days followed by prostatectomy within 7 days of the last figitumumab dose. There were no dose adjustments. Treatment was discontinued in the event of any serious adverse reaction. Patients did not receive any androgen deprivation or non-steroidal anti-androgen therapy. Patients were assessed with a history and physical examination, and
laboratory tests (complete blood count, serum creatinine, electrolytes, bilirubin, AST, ALT, bilirubin, gamma-glutamyltransferase, glucose, PSA and testosterone, IGF-I, IGF-II, and C-Peptide) at baseline, prior to each figitumumab infusion, and post-operatively (at 1-2 weeks and 3, 6 and 12 months). Blood samples were taken at baseline and pre-surgery for measurement of IGF-IR on circulating granulocytes by quantitative flow cytometry.

**Plasma and Tissue Figitumumab Concentrations**

Figitumumab plasma and prostate tissue concentrations were quantitatively determined using a validated enzyme linked immunosorbent assay (ALTA Analytical Laboratory, San Diego, California). The plasma sample was collected pre-operatively (within 24-hours). Approximately 1 cm$^3$ of the prostatectomy specimen was collected and immediately frozen on dry ice. All samples were stored at $-80^\circ$C until analysis.

**Tissue Analyses**

Immunohistochemistry staining was conducted by Ventana autostainer model Discover XT$^{TM}$ (Ventana Medical System, Tucson, Arizona) with enzyme labeled biotin streptavidin system and solvent resistant DAB Map kit by using androgen receptor (sc-816), IGF-IR (sc-713), and phospho-IGF-IR (sc-101703) antibodies (Santa Cruz biotechnology Inc., Santa Cruz, California); and phospho-AKT/Ser473 (3787), phospho-p44/42 MAPK (Erk1/2) (4376), and phospho-S6 (5364) antibodies (Cell Signaling Technology Inc., Danvers, Massachusetts). Using a categorical compositional scoring method, the sum of intensity level multiplied by percentage of cells at each intensity
level was calculated. Values on a four-point scale were assigned to each immunostain. Descriptively, 0 represented no staining by any tumor cells; 1 represented a faint or focal, questionably present stain; 2 represented a stain of convincing intensity; and 3 a stain of strong intensity. The overall score was determined as follows: overall score = 
\[(\% \text{ cells with visual score 1}) \times 1\] + 
\[(\% \text{ cells with visual score 2}) \times 2\] + 
\[(\% \text{ cells with visual score 3}) \times 3\]. Quantitative digital image analysis was performed using Image-Pro Plus version 4.5.1.22 (Media Cybernetics, San Diego, California). FISH was performed on FFPE prostate tissue using a commercial PTEN/CEP 10 dual-color probe (Vysis, Abbott Laboratories, Des Plaines, Illinois). PTEN copy number was determined by counting the number of probe signals in 200 non-overlapped, intact, interphase nuclei in each sample, of which 100 are tumour nuclei and 100 are non-tumour nuclei as controls. Hemizygous PTEN deletion was defined as greater than 30% (mean ± 2 SD in the non-tumour nuclei controls) of nuclei containing one PTEN signal in the presence of CEP 10 signals. Homozygous PTEN deletion was defined as greater than 20% of nuclei containing no PTEN signals in the presence of CEP 10 signals (26).

**Statistical Considerations**

The primary endpoint of this study was the biologic response rate, defined as the proportion of patients with inhibition of IGF-IR expression as determined by immunohistochemistry (IHC) analysis of the prostatectomy specimen. The rate of positive expression of IGF-IR in human prostate cancer is reported at 90-100% with a mean IHC score of 1.4 to 2.2 (out of 3) (10). A biologic response rate of >30% staining inhibition was considered of interest. Using a single stage design, a total of 14 evaluable subjects were planned to be enrolled. Patients not completing 3 cycles of protocol
therapy were to be replaced. The alpha level of the design was 0.05 and the power 0.9. Differences in pharmacodynamic parameters from pre-treatment to post-treatment specimens were evaluated using a paired t-test. Inter-group comparisons were compared using a student t-test for categorical variables. All reported P-values are two-sided.

RESULTS

Patient Characteristics

Sixteen patients were accrued from July 2008 to October 2009. Baseline characteristics are listed in Table 1.

Treatments Administered and Adverse Events

Fourteen patients received all planned 3 cycles of therapy. Two patients received only 1 cycle: one patient requested to be removed from protocol therapy, another patient develop Common Toxicity Criteria for Adverse Events (version 3.0) grade 3 hyperglycemia. This latter patient had a pre-existing history of type 2 diabetes on oral hypoglycemic medications and required the temporary addition of insulin to establish glycemic control. Otherwise, patients only experienced grade 1 and 2 adverse events (Table 2). There were no post-operative complications. The median time from last dose to surgery was 6 days (range 2-7) for patients receiving all 3 cycles of figitumumab. The two patients who received only 1 cycle of therapy had surgery 41 and 62 days post-figitumumab dosing.
Serum PSA and Testosterone

Median PSA at baseline was 7.2 µg/L (range 2.5-35) which declined to 4.45 µg/L (1.1-13) pre-operatively. Fifteen patients (94%) experienced a PSA decline of ≥25%, and 5 (31%) patients had a PSA decline of ≥ 50%. A waterfall plot of maximal percentage PSA decline by patient is shown in Figure 1. Mean serum testosterone at baseline was 13.7 nmol/L (range 5.1-21, standard deviation (SD) = 3.6). After cycle 1 of figitumumab, serum testosterone decreased in all patients by approximately 50% to a mean level of 7.2 nmol/L (range 3.1-11.0, SD = 2.5, P < 0.0001) and remained at that level for the duration of treatment, although no patient had a decrease to castrate concentrations (defined as 1.7 nmol/L). Serum testosterone recovered to baseline levels by 6 months (mean testosterone = 13.8, range 8.7-19, SD = 3.2).

Figitumumab Concentrations

In plasma, the mean pre-operative figitumumab concentration was 350.4 µg/ml (SD = 142.8, N = 13). Considering only patients who received all 3 cycles, the mean concentration was 406.1 µg/ml (SD = 46.7, N = 11). The figitumumab concentration in prostate tissue was roughly 8-fold lower at 51.3 µg/g (SD = 13.6, N = 14).

Pharmacodynamic Studies

Serum IGF Levels and Granulocyte Expression of IGF-IR

Mean serum IGF-I at baseline was 196.2 ng/ml (SD = 41.8) which increased significantly by approximately 5-fold to 952.8 ng/ml (SD = 246.7, P < 0.001) after
figitumumab. C-Peptide also increased significantly by 2 fold (mean baseline = 3.7 ng/ml (SD = 2.0), pre-operatively = 8.5 (SD = 3.7), P = 0.001) as did serum IGF-II levels to a lesser extent (mean baseline = 1540.4 ng/ml (SD = 311.5), pre-operatively = 1963.1 ng/ml (SD = 314.7), P < 0.001). The mean percentage change in granulocyte expression of IGF-IR was -34% (SD=21, range +17% to -54%, P=0.0001) as determined by quantitative fluorescence.

**Biopsy and Prostatectomy Tissue Assessments**

IGF-IR expression was determined in biopsy and matched prostatectomy specimens (N=16) (Figure 2). The mean immunohistochemistry visual score was 2.1 (SD = 0.6) in the core biopsy specimens and 1.1 (SD = 0.5) in the prostatectomy specimens (P < 0.0001) (Figure 3). The mean percentage of cells that had 0 or 1 staining (no staining or faint or focal, questionably present stain) was 19.4% (SD = 26.2%) in the biopsy specimens and 74.4% (SD = 28.5%) in the prostatectomy specimens (P<0.0001). Automated image analysis produced similar results with a positive IGF-IR staining area of 23.4% (SD = 14.3%) in the biopsy samples and 4.5% (SD = 5.8%) in the prostatectomy specimens (P=0.0002) (Figure 3). Fourteen patients (88%) had a decrease in IGF-IR staining in the prostatectomy specimen and 1 patient had “stable” staining (visual overall score 2.0 in biopsy and 2.1 prostatectomy tissue). Phospho-IGF1R expression was lower in the prostatectomy specimens compared to the biopsy specimens (N=16) by mean visual overall score (0.6 (SD = 0.7) vs. 1.2 (SD = 0.7) respectively, P=0.0294) and by percentage cells with no staining (64.4% (SD = 34.0%) vs. 16.9% (SD = 23.9%) respectively, P=0.0001) (Figure 3).
Downstream components of the IGF signalling axis were also evaluated with immunohistochemistry. Phospho-AKT visual overall score was not significantly different although there was a trend for more cells with negative staining in the prostatectomy specimens as compared to biopsy tissues (18.1% (SD = 34.1%) vs. 1.9% (SD = 7.5%) respectively, P=0.09, N=16). Eleven matched specimens were available for phospho-p44/42 MAPK immunohistochemistry. There was a trend for a lower overall score for phospho-p44/42 MAPK in the radical prostatectomy specimens compared to biopsy (1.1 (SD = 1.0) vs. 1.6 (SD=0.8), P=0.092) although the number of cells with no staining was higher statistically (55.5% (SD = 38.8%) in prostatectomy vs. 15.5% (SD = 27.0%) in biopsy, P=0.0279). Staining for phospho-S6 and Ki67 proliferation index (N = 13) was not different in the pre- and post- treatment tissues (P= 0.87 and P=0.24, respectively).

Immunohistochemistry staining for androgen receptor was significantly decreased in the prostatectomy specimens compared to pre-treatment biopsy (Figure 2). Matched biopsy and prostatectomy specimens could be compared in 14 patients. Mean visual overall score was 2.7 (SD = 0.4) in the pre-treatment biopsy specimen and predominantly nuclear, with a global decrease in staining with a mean visual overall score of 1.6 (SD = 0.6) in the prostatectomy tissues (P=0.0003) (Figure 3). The mean percentage of cells with no staining for androgen receptor was 2.9% (SD=6.1%) in the biopsy and 20% (SD= 20.4%) in the prostatectomy tissues (P=0.009).

Nine patients had hemizygous PTEN deletions and 1 patient had a homozygous deletion (N=16). Presence of a hemizygous or homozygous PTEN deletion did not appear to have any association with IGF-IR baseline or changes in expression, or PSA declines.
Only one patient appeared to have an increase in IGF-IR staining with the visual overall score being 1.5 in the biopsy and 1.9 in the prostatectomy specimen. Androgen receptor staining was also similar in the biopsy and prostatectomy specimen (visual overall score 1.6 for both). This patient had a hemizygous PTEN deletion, figitumumab prostate tissue concentration above the mean (57.0 µg/ml) and experienced a decline in PSA by 63% from baseline. The one patient who did not experience a PSA decline (PSA increased by 22%) had a decrease in IGF1R staining score from 2.0 to 1.4, a decrease in androgen receptor staining from 3.0 to 2.2, a hemizygous PTEN deletion, and prostate tissue concentrations of figitumumab below the mean (33.4 µg/ml).
DISCUSSION

In this study, the pre-operative administration of figitumumab allowed us to evaluate figitumumab concentrations in plasma and target cancer tissue and define changes in the IGF-IR pathway in all enrolled patients. Figitumumab concentrations in prostate tissues were roughly 87% lower than in concurrently sampled plasma, but still exceeded concentrations associated with activity in tumor xenografts (EC$_{50}$ 15 ug/ml) (20). After figitumumab treatment, we observed significant decreases in IGF-IR expression and a trend for decreasing downstream signalling pathway components, demonstrating the biologic activity of figitumumab in target cancer tissue. Previous studies with figitumumab have shown effects on IGF-IR expression on circulating granulocytes, which were also seen in this study. We also observed increasing serum levels of IGF-I and IGF-II, reflecting compensatory endocrine responses to receptor down regulation, and increasing serum C-peptide levels, indicative of increased insulin production, reflecting another compensatory response related to insulin resistance that arises secondary to elevations in growth hormone caused by IGF-I receptor blockade (27).

While blockade of IGF signalling may directly influence cell survival in a manner independent of steroid hormone signalling, there is also complex cross-talk between androgen and IGF signalling that may be relevant to our findings. IGF-IR signalling has been associated with the expression and activation of the androgen receptor through Foxo1, beta-catenin, and PI3K/AKT even in the presence of androgens (16, 28, 29). In line with those in vitro findings, we observed a marked decrease in androgen receptor expression associated with figitumumab treatment. This effect of IGF-IR targeting on
androgen receptor expression by prostate cancer cells may represent a mechanism of anti-tumor activity underlying the high proportion of the patients that experienced a PSA decline on this study. At the systemic level, serum testosterone was observed to decrease significantly on figitumumab treatment, a finding consistent with prior research associating IGF-I signalling and Leydig cell testosterone production (30). This may also account for some of the PSA declines observed in our study, although the decrease in testosterone was relatively modest and not to castrate levels. Recently, insulin has been shown to increase de novo steroidogenesis in prostate cancer cells (31) although in vivo studies have shown no effects of IGF-IR blockade on intra-tumoral androgen levels (32).

The degree of PSA declines observed in our study of patients without prior or concurrent hormone therapy is in contrast to results with IGF-IR targeting in patients with castration resistant prostate cancer. Cixutumumab, another fully human monoclonal antibody against IGF-IR, has been tested as a single agent in patients with CRPC, but clinical activity was modest with only 3 of 31 patients experiencing a PSA reduction (33). Pre-clinical data suggests that IGF-IR inhibition results in differential effects in androgen dependent and independent models, with induction of apoptosis in the former while only cell cycle arrest in the latter (23), perhaps explaining in part the differences in PSA declines seen in this study of men with treatment naïve, castrate sensitive disease. Furthermore, the development of castration resistant disease has been associated with increased androgen receptor expression including by gene amplification (34) and it is possible that IGF-IR signalling effects on androgen receptor expression may be less relevant in that context. Thus, further development of IGF-IR
targeted agents in prostate cancer may be best directed to patients with early, castrate sensitive disease. A randomized phase 2 study being conducted by the Southwest Oncology Group evaluating Cixutumumab in metastatic castration naïve patients is underway and will test the hypothesis whether the addition of IGF-IR inhibition therapy improves the efficacy of hormone therapy (clinicaltrials.gov identifier NCT01120236). Given the role of persistent androgen receptor signalling in CRPC, rational combination strategies of IGF-IR targeting with next generation hormone therapy such as abiraterone acetate (35) and MDV-3100 (36) should also be explored.

A limitation of this study is the lack of a randomized untreated control group, as the inherent differences in the tissue collection process between biopsies and radical prostatectomy specimens could potentially have an effect on gene expression. However, IGF-IR immunohistochemistry results in the pre-treatment biopsies on this study was consistent with IGF-IR staining in prostatectomy specimens in previously published reports, which supports the robustness of these results. There was also inconsistency between pharmacodynamic effects and PSA declines including one patient who had a PSA increase despite decreased IGF-IR and androgen receptor expression. Although this discrepant observation could be an indication of a cancer that is driven independently of IGF-IR signalling, these results could also be a reflection of the small sample size, brief duration of study treatment, the semi-quantitative immunohistochemistry evaluation and limitations of PSA as a clinical endpoint.

In summary, using pre-operative administration of figitumumab, we were able to document that a dose of 20 mg/kg administered every three weeks resulted in plasma and tissue concentrations sufficient to lead to biologic effects as estimated by
pharmacodynamic endpoints. Clinical activity was also observed, with a high proportion of patients having PSA declines. This supports the hypothesized role of IGF signalling in prostate cancer development and progression and justifies further clinical trials targeting this pathway.
REFERENCES


FIGURE AND TABLE LEGENDS

Figure 1. Waterfall plot of greatest percent PSA decline from baseline (columns represent individual patients).

Figure 2. Representative sections from pre-treatment prostate biopsy and post-treatment prostatectomy specimens for IGF1R (panel A: biopsy, panel B: prostatectomy) and androgen receptor (panel C: biopsy, panel D: prostatectomy) expression by immunohistochemistry.

Figure 3. IGF-IR (Visual Score, Panel A; Automated Image Analysis, Panel B), phospho-IGF-IR (Panel C) and androgen receptor (Panel D) expression by immunohistochemistry from pre-treatment prostate biopsy and post-treatment prostatectomy specimens (error bars represent +/- 1 SD).

Table 1. Patient Characteristics.

Table 2. Related Adverse Events.
Figure 1. Waterfall plot of greatest percent PSA decline from baseline (columns represent individual patients).
Figure 2. Representative sections from pre-treatment prostate biopsy and post-treatment prostatectomy specimens for IGF1R (panel A: biopsy, panel B: prostatectomy) and androgen receptor (panel C: biopsy, panel D: prostatectomy) expression by immunohistochemistry.
Figure 3. IGF-IR (Visual Score, Panel A; Automated Image Analysis, Panel B), phospho-IGF-IR (Panel C) and androgen receptor (Panel D) expression by immunohistochemistry from pre-treatment prostate biopsy and post-treatment prostatectomy specimens (error bars represent +/- 1 SD).
Figure 3 (Continued).

C

![Bar chart with error bars](image)

P = 0.0294

D

![Bar chart with error bars](image)

P = 0.0003
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (Range)</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>63 (50-71)</td>
<td></td>
</tr>
<tr>
<td>PSA, ng/ml</td>
<td>7.2 (2.1-35)</td>
<td></td>
</tr>
<tr>
<td>Clinical stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>Pathologic stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>T3</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Biopsy Gleason Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Prostatectomy Gleason Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Adverse Event</td>
<td>Number of Patients</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>--------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GRADE 1</td>
<td>2</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypersensitivity reaction</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Skin rash/dryness/pruritis</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Flu-like syndrome</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bowel Urgency</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
Clinical Cancer Research

A Phase 2 Pharmacodynamic Study of Pre-operative Figitumumab in Patients with Localized Prostate Cancer

Kim N. Chi, Martin E Gleave, Ladan Fazli, et al.

Clin Cancer Res Published OnlineFirst May 2, 2012.

Updated version
Access the most recent version of this article at:
doi:10.1158/1078-0432.CCR-12-0482

Author Manuscript
Author manuscripts have been peer reviewed and accepted for publication but have not yet been edited.

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, use this link http://clincancerres.aacrjournals.org/content/early/2012/05/02/1078-0432.CCR-12-0482. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.