Panel discussion: Management of Prostate cancer

History

- A 65-year-old male patient initially presented with severe back pain .
- The patient was evaluated and diagnosed with adenocarcinoma of the prostate with bone metastasis after undergoing FDG PET/CT.
- Prostate needle biopsy revealed adenocarcinoma of the prostate with a Gleason score of 8 (4+4).
- PSA > 100 ng/ml
- **How would you manage this patient?**

Discussion questions

- ADT---how to choose
- Any role of germline or somatic homologous recombination repair (HRR) testing (tissue Vs Liquid)
- What is your experience with genetic testing?
- Do you add next generation hormonal agents (NHA) or chemo in every patient of HSPC?

Further Management

- He was treated with **goserelin acetate injection and bicalutamide tablets for ~4 months**.

- **WHAT COULD HAVE BEEN BETTER APPROACH ?**

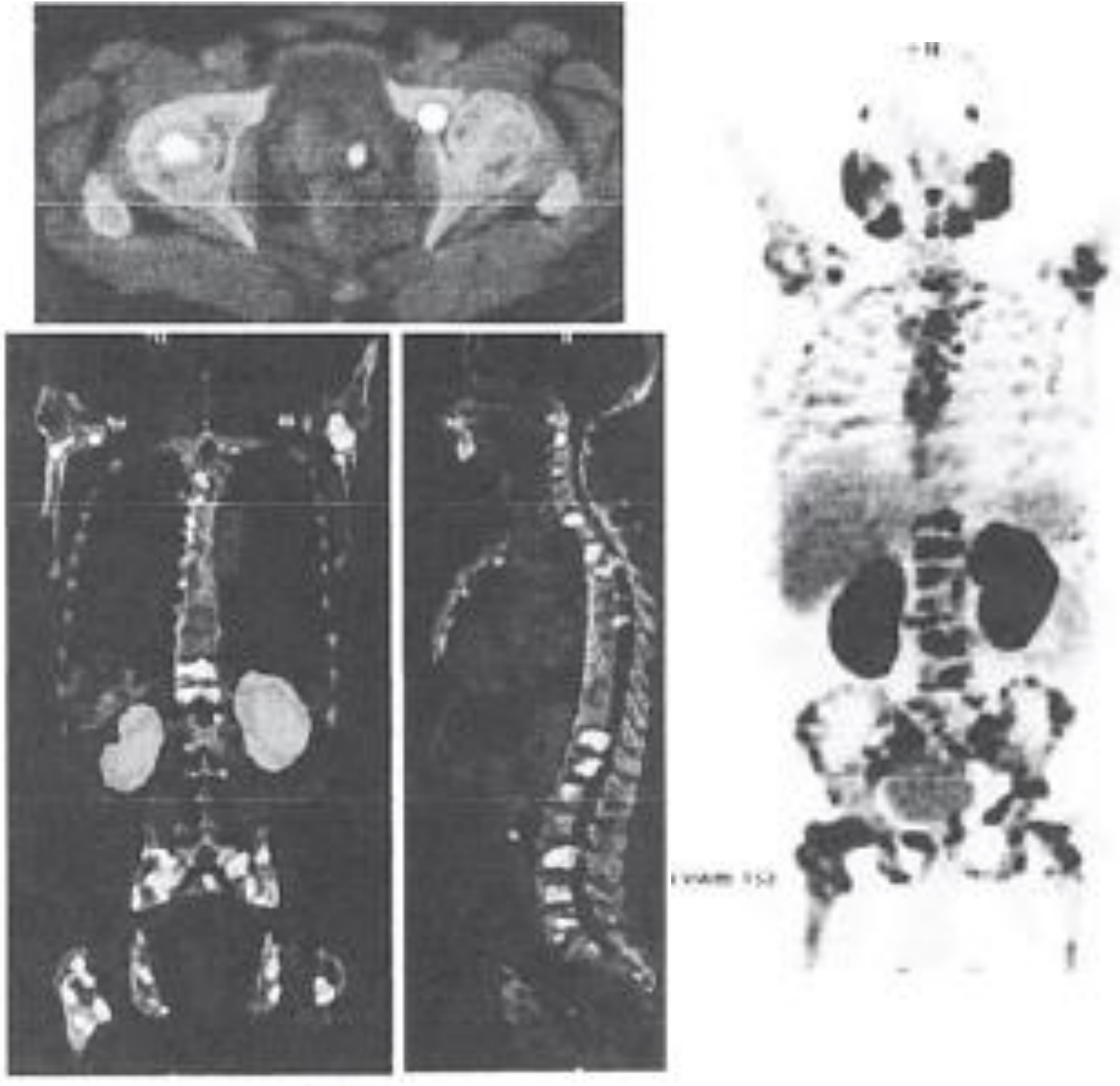
- Reassessment was performed after 4 months.

- The patient had an ECOG PS1
- PSA 10 ng/ml
- After 9 months again ---

- A Ga-68 prostate-specific membrane antigen (PSMA) PET/CT scan revealed post-TURP changes, with small mild nodular hypermetabolism in the left posterior peripheral zone, likely representing **residual prostatic disease.**

- The PSMA revealed extensive **FDG-avid heterologous osteosclerotic lesions** (Fig. 1), with a standardized uptake value (SUV) of 10.5 for the prostate and 18.0 for skeletal lesions.

Ga-68 PSMA PET CT scan



Further Management?

- PSA 66 ng/ml.
- The cardiac function was normal, with an ejection fraction of 62%.
- The blood counts were within normal limits.
- How to label CRPC?

- What else you want to know before managing ?

- **How would you manage this patient now?**

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[iii,kkk,lll]

No prior docetaxel/no prior novel hormone therapy[mmm]

- Preferred regimens
  - Abiraterone[u,nnn] (category 1[ooo])
  - Docetaxel[fff,ppp] (category 1)
  - Enzalutamide[u] (category 1)
- Useful in certain circumstances
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Sipuleucel-T[fff,qqq] (category 1)
- Other recommended regimens
  - Other secondary hormone therapy[u]

Prior novel hormone therapy/no prior docetaxel[mmm,sss]

- Preferred regimens
  - Docetaxel (category 1)[fff]
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Olaparib for HRRm (category 1)[ttt]
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Rucaparib for BRCA mutation[uuu]
  - Sipuleucel-T[fff,qqq]
- Other recommended regimens
  - Abiraterone[u,nnn]
  - Abiraterone + dexamethasone[nnn,vvv]
  - Enzalutamide[u]
  - Other secondary hormone therapy[u]

Prior docetaxel/no prior novel hormone therapy[mmm]

- Preferred regimens
  - Abiraterone[u,nnn] (category 1)
  - Cabazitaxel[fff]
  - Enzalutamide[u] (category 1)
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[fff]
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Sipuleucel-T[fff,qqq]
- Other recommended regimens
  - Other secondary hormone therapy[u]

Prior docetaxel and prior novel hormone therapy[mmm,sss]

- Useful in certain circumstances
  - Lutetium Lu 177 vipivotide tetraxetan (Lu-177–PSMA-617) for PSMA-positive metastases (category 1)[www]

(The following systemic therapies are category 2B if visceral metastases are present)

- Preferred regimens
  - Cabazitaxel[fff] (category 1[ooo])
  - Docetaxel rechallenge[fff]
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[fff]
  - Olaparib for HRRm (category 1[ooo])[ttt]
  - Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[fff]
  - Radium-223[rrr] for symptomatic bone metastases (category 1[ooo])
  - Rucaparib for BRCA mutation[uuu]
- Other recommended regimens
  - Abiraterone[u,nnn]
  - Enzalutamide[u]
  - Other secondary hormone therapy[u]

Further course

- Chemohormonal therapy was planned, and the patient was admitted for the first cycle of chemotherapy.
- **docetaxel 120 mg, denosumab 120 mg and continued goserilin acetate.**
- **conventional docetaxel 120 mg after premedication with corticosteroids and antihistamines**.
- The patient developed an **anaphylactic reaction (bronchospasm, hypotension and skin rash)** within 5 min; he was administered an IV injection of chlorpheniramine maleate (Avil), hydrocortisone and paracetamol, and recovered within 30 min.
- **How would you manage this patient now?**

Discussion questions

- 2 weekly or 3 weekly docetaxel?
- What is the average no of cycles of docetaxel received in your patients?

Discussion question

- Will you use cabazitaxel in this patient or switch to NHA?

Discussion question

- Which are the most troublesome problems with conventional docetaxel?

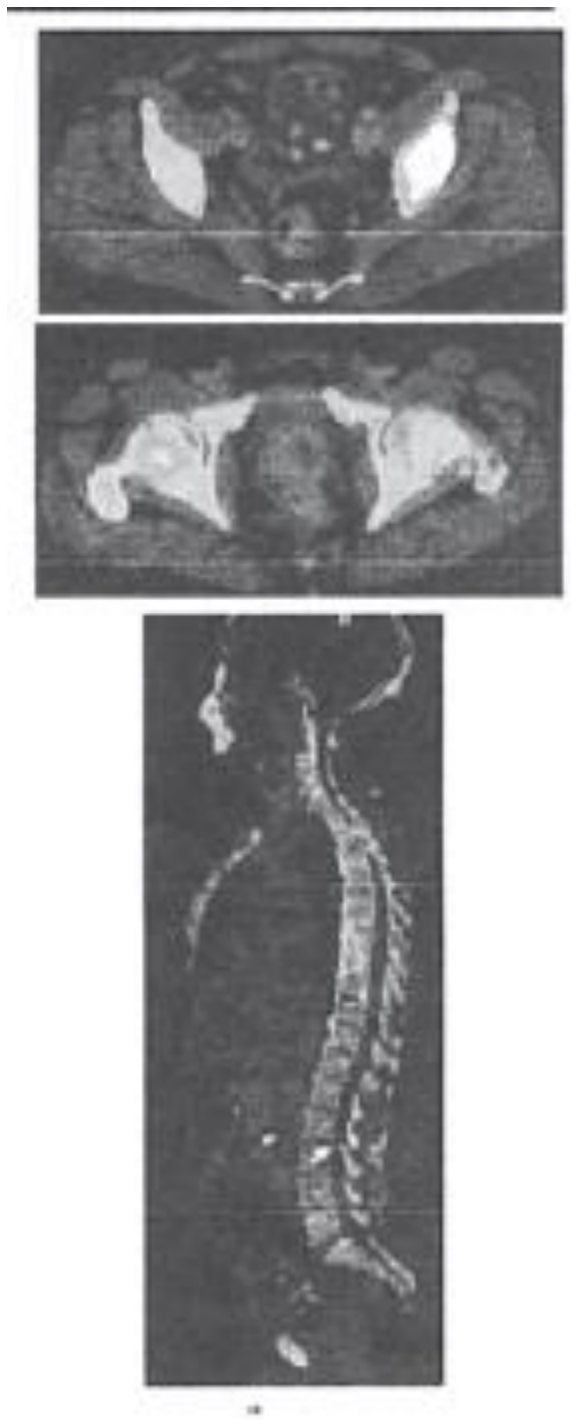
Discussion questions

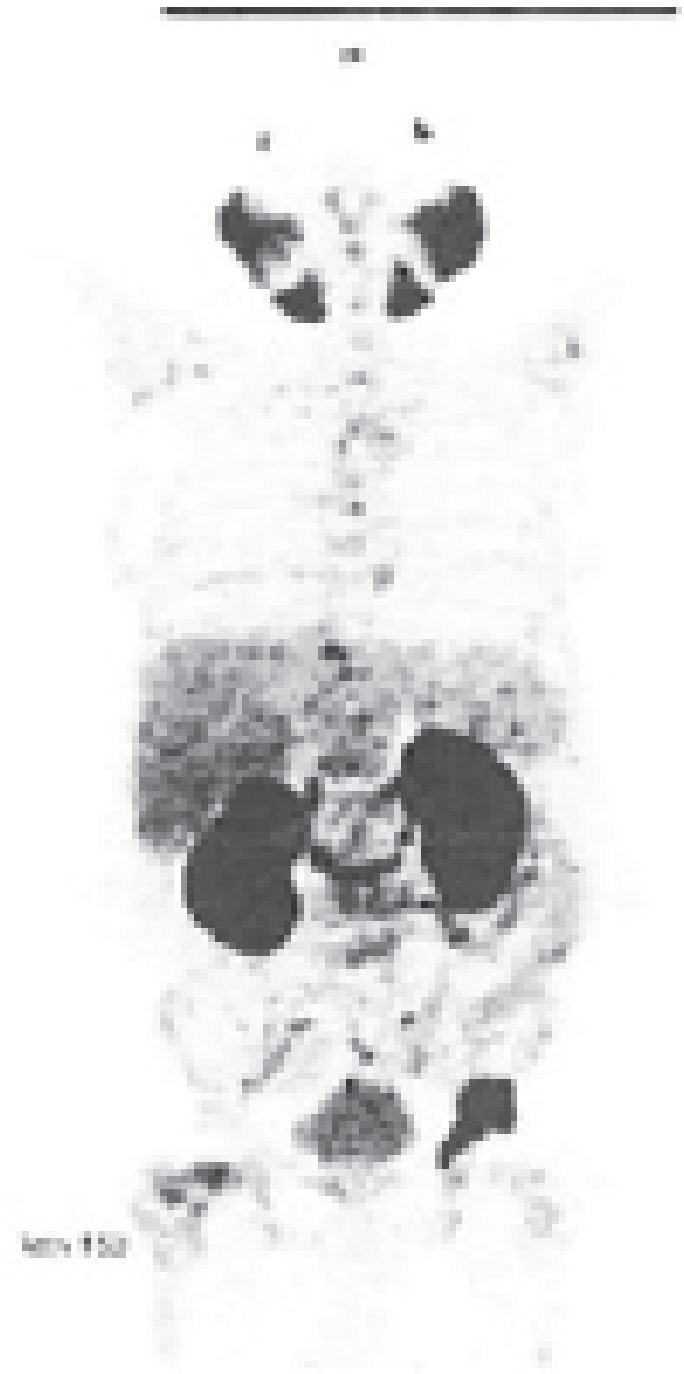
- What fraction of patients who are eligible for docetaxel do you use novel formulation in your clinical practice?
- What is the max no of cycles for which you have used NDLS in your patients?

Further course

- Next day, the patient received **120 mg of the Nanosomal docetaxel lipid suspension (NDLS),** which was well-tolerated without any adverse reactions.
- The patient subsequently received the next **4 cycles** of chemotherapy with Doceaqualip.
- A reassessment examination performed after the forth cycle of chemotherapy with a Ga-68 PSMA PET/CT scan showed **mild interval regression** of the small mild nodular hypermetabolism in the left posterior peripheral zone and morphologically stable heterogenous osteosclerotic lesions with internal regression of the metabolic activity.
- However, mild interval progression of focal hypermetabolism in the left acetabulum was present.
- No new metastases were observed, with an SUV of 6.9 for the prostate and 19.4 for the skeletal lesions.

Ga-68 PSMA PET CT scan





Further course

- The patient tolerated the Doceaqualip treatment well, without any adverse events.

- The patient received 8 cycles of Doceaqualip, denosumab 120 mg, goserelin with filgrastim 300 µg.
- PSA -12 ng/ml
- Repeat PSMA PET –further regression and no new lesions .
- WHAT TO DO NOW ?
- HOW MANY CYCLES ?

Hindawi
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Research Article

A Multicentric, Retrospective Efficacy and Safety Study of Nanosomal Docetaxel Lipid Suspension in Metastatic Castration-Resistant Prostate Cancer

Aseem Samar,[1] Srikant Tiwari,[2] Sundaram Subramanian,[3] Nisarg Joshi,[4] Jaykumar Sejpal,[4] Mujtaba A. Khan,[4] and Imran Ahmad [5]

Results

- Data of 24 patients with mCRPC were analyzed in this study.

- NDLS was administered as a 2-weekly regimen in 37.5% (9/24; all first-line) patients and as a 3-weekly regimen in 62.5% patients (15/24)

Samar A et al. Prostate Cancer. 2020 Nov 24;2020:4242989

Demographic and baseline characteristics (N=24)

Characteristics	2-weekly NDLS ($n=9$)	3-weekly NDLS ($n=15$)
Age (years), *n* (%)		
<65 years	2 (22.22)	7 (46.67)
65–74 years	3 (33.33)	4 (26.67)
≥75 years	4 (44.44)	4 (26.67)
Baseline BSA (median (range))*	1.7 (1.5–1.9)	1.7 (1.2–1.9)
Median follow-up duration, months (range)	14.7 (5.5–25.7)	12.2 (7.9–15.6)
ECOG performance score, *n*		
0	5 (55.55)	3 (20)
1	3 (33.33)	8 (53.33)
2	1 (11.11)	2 (13.33)
3	0	2 (13.33)
Gleason score at initial diagnosis		
≤7	4 (44.44)	13 (86.67)
8	1 (11.11)	2 (13.33)
≥9	2 (22.22)	0
Unknown	2 (22.22)	0
Median PSA at baseline, (range), ng/mL	226 (18.17–510)	28 (1.6–2030)
Median baseline Hb (range)	10.9 (9.8–12.7)	10.8 (8.2–13.1)
Metastasis site		
Bone	7 (77.77)	15 (100)
Unknown	2 (22.22)	0
Previous therapy		
Radiotherapy	3 (33.33)	4 (26.67)
Prostatectomy	5 (55.55)	12 (80)
Orchiectomy	4 (44.4)	11 (73.3)
Previous systemic therapy		
Bicalutamide	0	4 (26.67)
Abiraterone	0	8 (53.33)
Comorbidities**		
Diabetes	2 (22.22)	6 (40)
Hypertension	0	7 (46.67)

Treatment delivery

Treatment	2-weekly NDLS ($N=9$)	3-weekly NDLS ($N=15$)
Cumulative dose (mg), median (range)	650 (240–1660)	500 (300–750)
No. of cycles, median (range)	14 (6–40)	10 (6–11)
Actual dose intensity (mg/m^2/week), median (range)	21.04 (20–37.50)	18.75 (16.67–25)
Relative dose intensity* (%), median (range)	84 (80–150)	75 (67–100)

*Calculated at a planned dose intensity of 25 mg/m^2/week.

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PSA response rate of NDLS chemotherapy

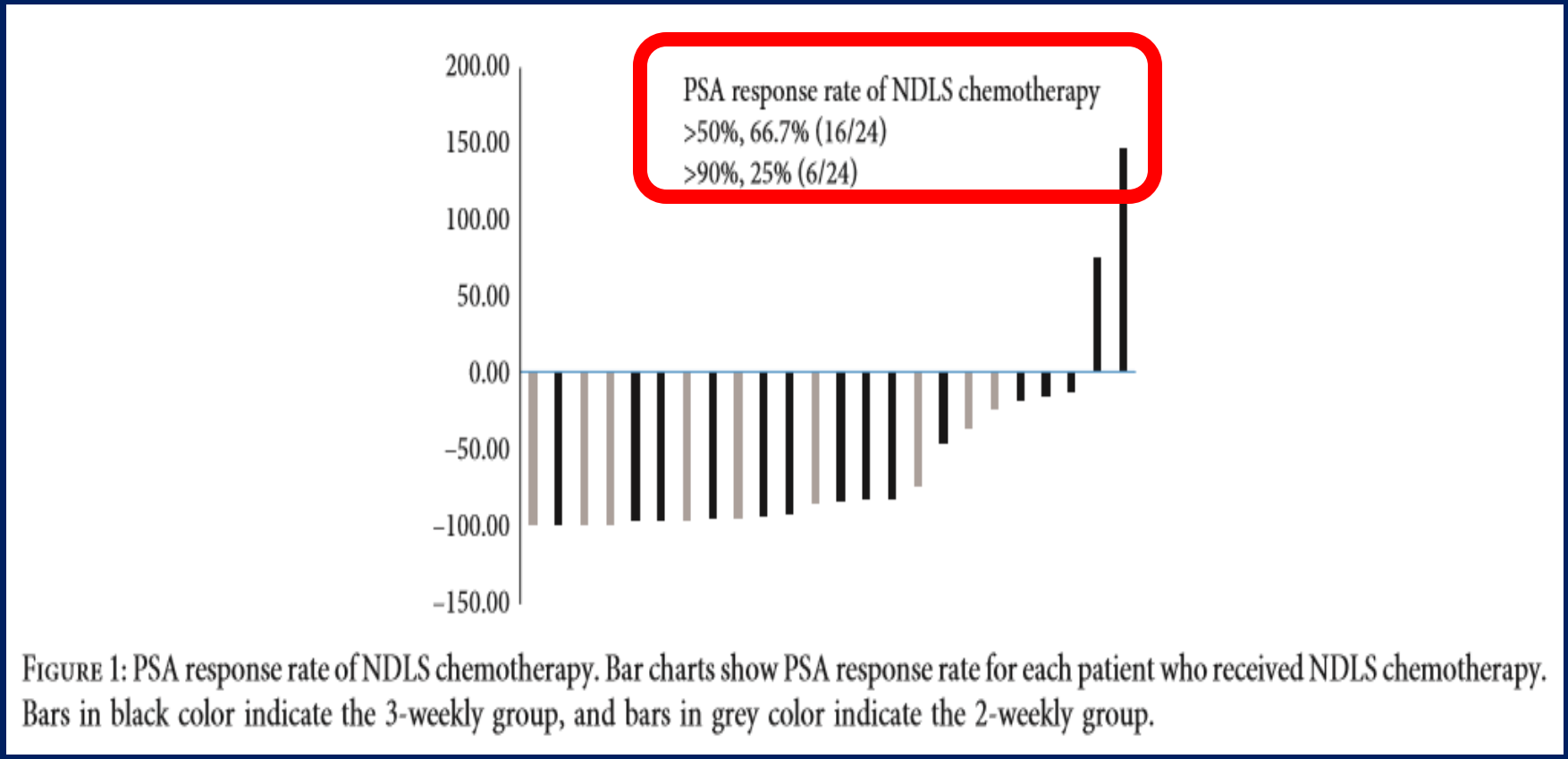

FIGURE 1: PSA response rate of NDLS chemotherapy. Bar charts show PSA response rate for each patient who received NDLS chemotherapy. Bars in black color indicate the 3-weekly group, and bars in grey color indicate the 2-weekly group.

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Efficacy evaluation

Parameter		2-weekly NDLS ($n=9$) (%)	3-weekly NDLS ($n=15$) (%)
PSA decline	PSA decline >50%	77.8%	60%
	PSA decline >90%	55.6%	40%
Median %PSA decline		96.31%	83.29%
Median TTF (days)		200	195
Therapy after NDLS treatment*	Abiraterone ($n=4$)	1	3
	Biculatamide** ($n=5$)	0	5
	Cabazitaxel ($n=1$)	1	0
	Cyclophosphamide ($n=1$)	0	1
	Enzalutamide ($n=2$)	1	1
	Mitoxantrone ($n=1$)	0	1

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Safety profile

AEs	2-weekly group ($N=9$)		3-weekly group ($N=15$)
	Grade I/II, *n* (%)	Grade III, *n* (%)	All grade I/II, *n* (%)
Hematological AEs			
Anemia	8 (88.89)	—	13 (86.67)
Lymphopenia	6 (66.67)	—	5 (33.33)
Thrombocytopenia	2 (22.22)	—	2 (13.33)
Neutropenia	3 (33.33)	2 (22.22)	—
Nonhematological AEs			
Nausea	1 (11.11)	—	4 (26.67)
Vomiting	1 (11.11)	—	6 (40)
Weakness	3 (33.33)	—	9 (60)
Hyperglycemia	1 (11.11)	—	—
Anorexia	—	—	1 (6.67)
Diarrhea	—	2 (22.22)	4 (26.67)
Alteration in LFT	—		1 (6.67)
Mouth ulcer	1 (11.11)	—	—
Constipation	2 (22.22)	—	6 (40)

Samar A et al. Prostate Cancer. 2020 Nov 24;2020:4242989

Conclusions

- Nanosomal docetaxel lipid suspension (NDLS) as 2-weekly and 3-weekly regimens was effective and well tolerated in managing patients with mCRPC

Samar A et al. Prostate Cancer. 2020 Nov 24;2020:4242989

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Case Report

Biweekly DoceAqualip in mCRPC patients beyond 20 cycles: A case series

J Oncol Pharm Practice
0(0) 1–5

DOI: 10.1177/10781552211008223
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SAGE

Tiwari S et al. J Oncol Pharm Pract. 2021 Apr

Introduction

- Docetaxel 75mg/m2 every 3weeks for up to 10 cycles is an accepted standard regimen in metastatic castration-resistant prostate cancer (mCRPC).
- The experience with >20 cycles of biweekly nanosomal docetaxel lipid suspension (NDLS) treatment in patients with mCRPC.is being reported here.
- Cases with long-term treatment of NDLS treatment in mCRPC patients were identified from the medical records of Jawaharlal Nehru Cancer Hospital & Research Centre Bhopal, India.
- A total of three cases with >20 cycles of NDLS are presented here.

Tiwari S et al. J Oncol Pharm Pract. 2021 Apr

Patient demographics & Efficacy

Parameters	Patient 1	Patient 2[a]	Patient 3
Age (years)	78	77	75
BSA (m^2)	1.5	1.8	1.8
ECOG score	0	0	1
Gleason score	3 + 4 (prostatic adenocarcinoma)	4 + 4 (prostatic adenocarcinoma)	5 + 5 (prostatic adenocarcinoma)
Metastatic sites	Bone (vertebra)	Bone (vertebra and pelvis)	Bone (vertebra and pelvis)
Line of therapy	I	I	II
No of NDLS cycles	22	36	40
Baseline Hb (g/dL)	10.7	12.5	11
Baseline PSA (ng/mL)	510	315.2	40
Nadir PSA (ng/mL)	2.56	41.92	1.05
PSA change from baseline (%)	99.50% (decrease)	86.70% (decrease)	97.38% (decrease)
Time to achieve Nadir, months	9.3	2.3	5.9
Number of cycles of NDLS given to achieve PSA nadir	14	6	13
Last PSA measured (ng/mL)	15.92	87.19	8.5
Cumulative NDLS dose (mg/m^2)	1015	1515	1660
Actual dose intensity (mg/m^2/week)	23.07	21.04	20.75
Relative dose intensity (%)	92	84	83
TTF, months	14.8	18.2	20.6
OS, months	21.6 months	22.2 months	25.8 months
Toxicities after 10 cycles	Anemia (grade 1)	Neutropenia (grade 3) Anemia (grade 1) Generalized weakness (grade 1)	Anemia (grade 1) Lymphopenia (grade 1) Hypoglycaemia (grade 1)

Tiwari S et al. J Oncol Pharm Pract. 2021 Apr

Management and outcomes

Overall, the 3 patients received biweekly NDLS at a dose of 45mg/m^2 for 22, 36, and 40 cycles, respectively, except for one patient where NDLS was initiated at 50mg/m^2 and later reduced to 45mg/m^2.

All the 3 patients reported a PSA response (>50% decline in PSA levels from baseline).

The time to treatment failure (TTF) was 14.8, 18.2, and 20.6months in these 3 patients, respectively.

PSA nadir occurred after 14, 6 and 13 cycles, respectively. The OS was 21.6, 22.2 and 25.8months, respectively.

Biweekly NDLS for >20 cycles was effective and well-tolerated in patients with mCRPC. NDLS can potentially be used for long-term management, which may be a requirement for most patients with mCRPC

Tiwari S et al. J Oncol Pharm Pract. 2021 Apr

Final comments by panelists


Thank You!