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Case Report A SciTechnol Journal

Influence of Long-term Abemaciclib, a New CDK 4/6 Inhibitor: Decrease in Liver Metastasis in a Patient Suffering from Metastatic Breast Cancer

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Abstract

An 82-year old patient suffering from metastatic breast cancer (FIGO IV D) underwent surgical operations and radiation treatments in the past. From November 29, 2018 until now, the patient was treated with 100 mg Abemaciclib (2 × 50 mg). During therapy, her pain subjectively decreased. No relevant side effects were observed. After 6 months, hepatic metastasis was checked by means of computer tomograph (CT) and a significant reduction of metastasis size was documented.

Keywords

CDK 4/6 inhibitor; Breast cancer; Continuous therapy; Metastasis reduction; Tumour reduction; Side effect

Introduction

In this paper we would like to report the therapy used to decrease hepatic metastasis in an 82 year old female patient who earlier underwent surgery and radiation therapy for metastatic breast cancer in 2013. The patient was again presented with hepatic metastasis in 2018; she refused chemotherapy but agreed for continuous oral therapy. Hence she was treated with Abemaciclib 50 mg 1 – 0 – 1.

Case Report

A 82-year-old female patient, 86 kg, 163 cm (BMI: 32.2), married, two children, non-smoker, living in a normal social milieu, diabetes mellitus II since 1998 (HbA1c 11/2018: 6.7%), renal insufficiency gr 3-4, only appendectomy as a previous operation, no hypertension, moderate combined valvular aortic stenosis, erosive osteochondritis and physical disability according to age.

In May 2013 the patient was R0-mastectomied, right-hand side, in a pT3+pTis pN1 mi (1/2sn), L0, V0, M0. R0. G2, estrogen-receptor and progesteron-receptor positive, Her-2 positive, invasive lobular, G2 breast cancer, initial Ki 67 was 5%. In addition, LIN and DCIS were detected.

In August 2013 the patient was treated by means of breast-preserving surgery, left-hand side, in a pT1c, pN0 (0/3sn), M0, R0, L0, V0, G2, estrogen-receptor and progesteron-receptor positive, Her-2 negative, Ki 67: 2%, invasive ductal (NST). In August, radiation of the breast was carried out on the left-hand side. The clinical diagnostics (thorical X-ray, sonography of the liver and scintigraphy of the skeleton) were negative. In May 2013, antihormonal therapy started with Letrozol 2.5 mg. The patient refused further therapy.

In November 2018, hepatic metastasis was observed. Sonographic punctation histology: metastasis of the further known mamma carcinoma (ER: +, PR: +, HER-2: -, Ki 67: 17%) (Figure 1).

The patient refused the chemotherapy offered but agreed to continuous oral therapy with Abemaciclib 50 mg 1 – 0 – 1.

After six months of oral therapy, 2 × 50 mg daily, her pain subjectively decreased continuously. No relevant side effects were observed. After six months, hepatic metastasis was controlled by computer tomograph (Figure 2).

The significant reduction in the previously described hepatic metastasis was a surprise finding.

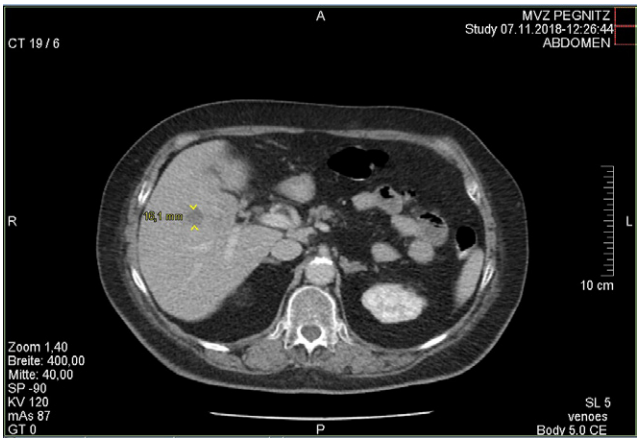

Figure 1: Computer tomography dated November 7, 2018: 16.1 mm intrahepatic metastasis was detected.

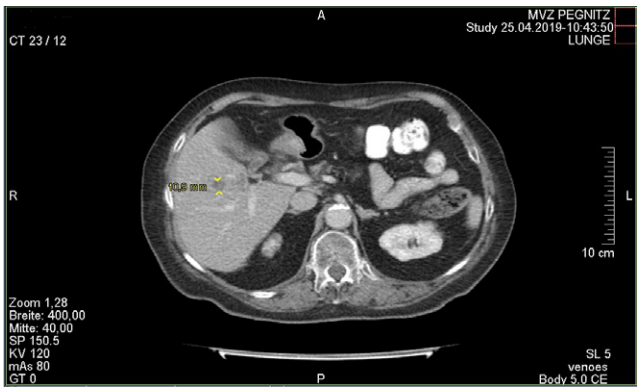

Figure 2: Computer tomography dated April 25, 2019: A significant reduction in metastasis size was documented at 10.9 mm.

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Discussion

After the introduction of the first effective drug combinations from the mid-1940s onwards, there was an improvement in the systemic treatment of oncological patients. In order to improve comparability, the therapies were standardized, and therapy in cycles of 21 days became increasingly established as the norm. In this way, it was possible to better compare the effectivity of known and new medications.

By means of individual reductions in doses, it was possible to demonstrate that certain substances had fewer side effects when administered on a weekly basis than on a three-weekly basis (e.g. Paclitaxel). At the same time, the effect on the tumour was sometimes more lasting. At the beginning of the 2000s, Imatinib – a tyrosine-kinase inhibitor – was the first sustainable therapy strategy involving medication to be taken on a daily basis.

A new group of cancer therapeutics are cyclin-dependent kinases (CDK) inhibitors. CDK-inhibitors control cellular proliferation [1,2]. Abemaciclib is a cyclin-dependent kinase 4 and 6 inhibitor [3-5]. It is very effective in patients with metastatic breast cancer in combination with fulvestrant and aromatase inhibitors [6-9].

We use Abemaciclib because it can be administered orally twice a day in self-medication.

We expected a moderate increase in the size of the hepatic metastasis of the breast cancer [10-12]. In a patient with metastatic breast cancer under cytotoxic therapy over such a long period of time, we also expected to see more severe side effects [13]. The regularly implemented laboratory examinations did not show changes requiring treatment (such as neutropenia anaemia and thrombopenia). The body's own repair and regeneration and mechanisms seem to compensate well for the cytotoxic effect. We were positively surprised to see that the patient reported a decline in upper abdominal pain. We were also surprised at the result of the control CT.

This clinical effect seems to be significant. On the one hand, side effects are moderate. On the other hand, oral administration every 12 hours seems to result in continuous plasma levels above the lower limit of the therapeutic index. In the event of continuous administration over several months, this apparently resulted in a lasting effect on the tumour.

Conclusion

It seems to be the case that although the higher doses are more effective, the more severe side effects result in most patients discontinuing the medication prematurely. For this reason it is not possible to observe an effect such as that observed by us.

While the therapeutic index of classic chemotherapeutics is very narrow, therefore requiring stringent dosing according to body surface, the therapeutic index of Abemaciclib seems to be much broader. We believe that the functioning of CDK 4/6 inhibitors is responsible for this effect.

Knowing this typical CDK 4/6 effect of Abemaciclib, it is important in assessing the therapeutic effect. In the future therefore, such clinical effects might be recorded in order to modulate Abemaciclib therapy. Further investigations are required.

References

1. Asghar U, Witkiewicz AK, Turner NC, Knudsen ES (2015) The history and future of targeting cyclin-dependent kinases in cancer therapy. Nat Rev Drug Discov 14: 130-146.
2. Malumbres M, Barbacid M (2009) Cell cycle, CDKs and cancer: A changing paradigm. Nature Reviews Cancer 9: 153-166.
3. Barroso-Sousa R, Shapiro GI, Tolaney SM (2016) Clinical development of the CDK4/6 inhibitors ribociclib and abemaciclib in breast cancer. Breast Care (Basel) 11: 167-173.
4. DeMichele A, Clark AS, Tan KS, Heitjan DF, Gramlich K, et al. (2015) CDK 4/6 inhibitor palbociclib (PD0332991) in Rbþ advanced breast cancer: Phase II activity, safety, and predictive biomarker assessment. Clin Cancer Res 21: 995-1001.
5. Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, et al. (2016) Ribociclib as first-line therapy for HR-Positive, advanced breast cancer. N Engl J Med 375: 1738-1748.
6. Dickler MN, Tolaney SM, Rugo HS (2017) MONARCH 1, a phase 2 study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2-metastatic breast cancer. Clin Cancer Res 23: 5218-5224.
7. Sledge GW Jr, Toi M, Neven P, Sohn J, Inoue K, et al. (2017) MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2-advanced breast cancer who had progressed while receiving endocrine therapy. J Clin Oncol 35: 2875-2884.
8. Goetz MP, Toi M, Campone M, Sohn J, Paluch-Shimon S, et al. (2017) MONARCH 3, Abemaciclib as initial therapy for advanced breast cancer. J Clin Oncol 35: 3638-3646.
9. Johnston S, Martin M, Di Leo A, Seock-Ah I, Ahmad A, et al. (2019) MONARCH 3 final PFS: A randomized study of abemaciclib as initial therapy for advanced breast cancer. NPJ Breast Cancer 5: 5.
10. Normanno N, Di Maio M, De Maio E, De Luca A, De Matteis A, et al. (2005) Mechanisms of endocrine resistance and novel therapeutic strategies in breast cancer. Endocr Relat Cancer 12: 721-747.
11. O'Leary B, Finn RS, Turner NC (2016) Treating cancer with selective CDK4/6 inhibitors. Nat Rev Clin Oncol 13: 417-430.
12. Patnaik A, Rosen LS, Tolaney SM, Tolcher AW, Goldman JW, et al. (2016) Efficacy and safety of Abemaciclib, an inhibitor of CDK4 and CDK6, for patients with breast cancer, non-small cell lung Cancer, and other solid tumors. Cancer Discov 6: 740-753.
13. Zorn O, Heirler F (2019) Influence of abemaciclib, a new CDK 4/6 inhibitor, decrease in potassium electrollytes and urea in a patient suffering from metastatic breast cancer. J Clin Exp Oncol 8: 1.

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